Neuroimaging Highlight

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The "Hot Cross Bun" Sign in Leptomeningeal Carcinomatosis

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The "hot cross bun" sign is seen on transverse T2-weighted magnetic resonance imaging (MRI) of the brain as a cruciform hyperintensity in the pons, which is classically associated with multiple system atrophy (MSA).[1] A 38-year-old woman was referred to our department with a one-month history of intermittent vomiting and a two-week history of diplopia. The patient reported having partial temporal lobe epileptic seizures or generalized epileptic seizures since the age of seven, which persisted despite receiving different antiepileptic drugs, including valproate, phenytoin, carbamazepine, diazepam, and so forth. She denied any remarkable family history. At admission, multiple large pigmented melanocytic skin lesions were noted on the patient's head, trunk, and extremities (Figure A and B). She reported that she was born with these lesions, which did not evolve after she grew up. Upon examination, the patient presented with right abducent nerve palsy with horizontal nystagmus; the Chaddock sign was positive bilaterally. Chest and abdominal computed tomography (CT) scans, gastroscopy, and abdominal and gynecological ultrasounds were all generally normal. A brain CT scanning revealed signs of atrophy in the cerebellum and brainstem (image not shown). Magnetic resonance imaging-T1 weighted image showed hyperintense lesions in the central pons (E and F). T2 weighted image displayed a typical "hot cross bun" sign and atrophy in the cerebellum and pons (G and H). Three brain MRI examinations were undertaken approximately six months apart did not show any evolution of the above-mentioned lesions. Additionally, no apparent perilesional edema, space-occupying, or contrast enhancement was revealed. "W" waves, which disappear in multiple system atrophy (MSA), were still present as detected by transcranial Doppler. Laboratory tests on blood, urine, live function, renal function, lipid profile, serum glucose level, thyroid hormones and parathyroid hormone were normal. Serum viral studies (HBV, HCV, HIV) and syphilis serology tests (rapid plasma regain) were all negative. The patient received serial lumbar punctures; increased cerebrospinal fluid (CSF) pressure (one was more than 400 mmH_2O), increased leukocytes, elevated protein levels, and decreased glucose concentrations were noted. Malignant melanoma cells were observed in CSF (Figure C and D).

Leptomeningeal carcinomatosis (LC) is a devastating complication of systemic cancer that occurs in patients with solid tumors, but is most often observed in patients with breast cancer, lung cancer, or melanoma. In this study, we identified a case of LC by finding malignant melanoma cells in CSF. Interestingly, the patient presented with atrophy of the cerebellum and brainstem, and exhibited typical "hot cross bun" sign in the pons, which are most often observed in patients with MSA.[1]

The "hot cross bun" sign may reflect Wallerian degeneration,[1] due to a selective loss of myelinated transverse pontocerebellar fibers and neurons in the pontine raphe with preservation of the pontine tegmentum and corticospinal tracts.[2] Further investigations revealed this sign reflects not only the loss of myelinated fibers and neurons, but also the gliosis of regions including the middle section of the reticular formation and the pontocerebellar fiber between the medial lemniscus and pyramidal tract, as well as the area of the pontocerebellar fibers that cross at the basis pontis.[3] Regardless of the mechanism, this pattern of selective fiber and neuron depletion results in a cross-shaped hyperintensity in the pons on T2-weighted images. Although the patient presented with typical radiologic appearance classically associated with MSA, we did not find adequate evidence to establish a diagnosis of MSA, such as Parkinsonism, or autonomous nerve dysfunction. The patient's symptoms and imaging findings were not preceded by any chemotherapies. Thus it appears unlikely that the "hot cross bun" sign was caused by chemotherapies. We speculate that the "hot cross bun" sign seen in this patient is due to neurodegeneration caused by leptomeningeal carcinomatosis. However, a possible association between epileptic seizures and this sign cannot be excluded.

The "hot cross bun" sign was initially considered to be specific for MSA; however, it seems not pathognomonic for MSA.[4] From the literature, it appears that the hot cross bun appearance on MRI may be seen in more disorders other than

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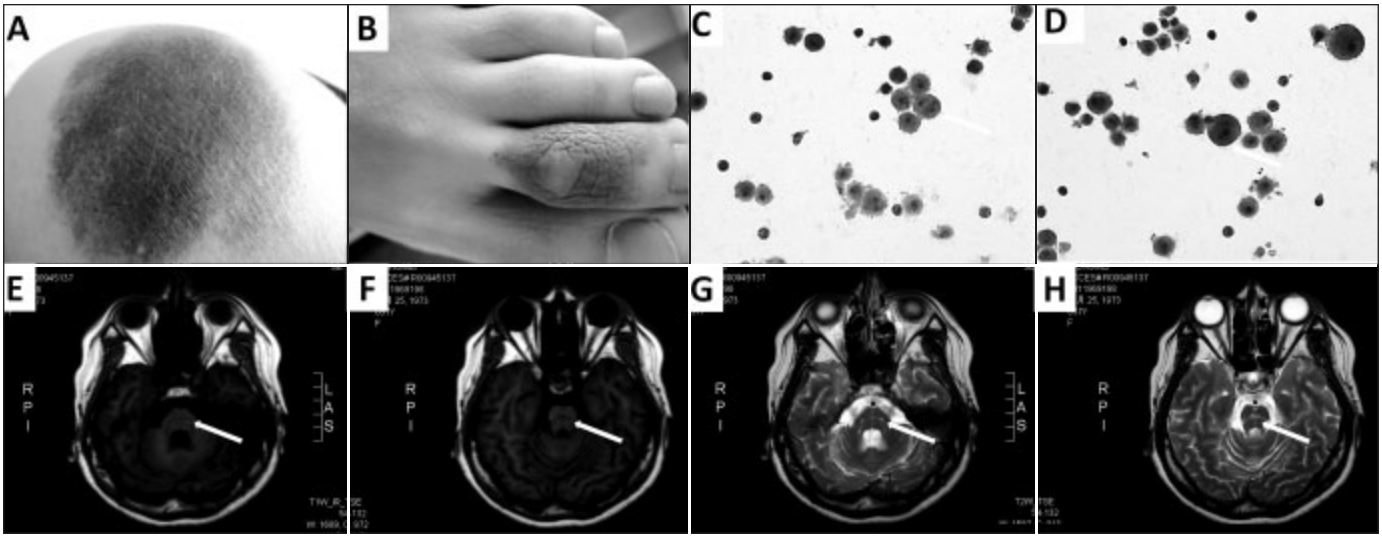

Figure: *Clinical manifestations and imaging findings. Melanocytic skin lesions on one shoulder (A) and foot (B). Malignant melanoma cells were found in cerebrospinal fluid (C and D, white arrows). T1WI shows hyperintense lesions in the central section of the pons (E and F). T2WI displayed a typical "hot cross bun" sign and atrophy in the pons (G and H). Three brain MRI examinations were undertaken approximately six months apart did not show any evolution of the above-mentioned lesions.*

MSA, including Creutzfeldt-Jakob disease (CJD), spinocerebellar ataxia, and progressive multifocal leukoencephalopathy (PML), vasculitis, etc.[5-9] In this case, we did not find any evidence pointing to a diagnosis of CJD, spinocerebellar ataxia, PML or vasculitis. To the best of our knowledge, the "hot cross bun" sign has not been reported in patients with LC. This case expands the spectrum of diseases that present with the "hot cross bun" sign.

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Authors' contributions

Study concept and design: Li Sun. Acquisition of data: Hong-Liang Zhang, Tao Jin and Haining Zhang. Drafting of the manuscript: Hongliang Zhang and Yongfang Tian. Authors HZ and YT contributed equally to the work.

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