(18F)-FDG PET/CT AND MRI IN DIAGNOSIS OF IDIOPATHIC LATE-ONSET CEREBELLAR ATAXIA

[1]Ara Kaprelyan, [2]Pavel Bochev, [1]Alexandra Tzoukeva, [1]Margarita Grudkova, [1]Borislav Ivanov, [3]Radoslav Georgiev, [1]Daniela Arabadjieva

[1]Department of Neurology and Neurosciences, [2]Depatment of Nuclear Medicine and Radiotherapy, and [3]Department of Roentgenology;

Faculty of Medicine, Medical University "Prof. P. Stoyanov"

55 Marin Drinov Street

9002 Varna,

Bulgaria E-mail: arakapri07@yahoo.co.uk

Telephone: +35952978313

Abstract

Adult-onset progressive cerebellar disorders can result from many pathological processes. The diagnosis is usually based on the medical history, neurological examination, laboratory investigations, and presence of cerebellar atrophy on CT and MRI. In addition, SPECT and PET have been used in detection of genetic and non-genetic ataxias. We studied the cerebral glucose metabolism and neurological dysfunction in 7 patients with late-onset cerebellar ataxia. All patients underwent (18F)-fluoro-2-deoxy-D-glucose (FDG) PET scanning with Phillips Gemini TF (16slice) PET/CT. The age at progressive cerebellar symptoms onset was over 45 years. Detailed medical history, physical findings and laboratory tests excluded other acquired causes of cerebellar ataxia. CT scans and MRI revealed presence of cerebellar and brainstem atrophy. (18F)-FDG PET showed moderate to severe cerebellar and brainstem hypometabolism. Based on our own clinical and neuroimaging findings, we support the notion that brain FDG PET scanning may be useful as a complimentary diagnostic tool in evaluation of patients with late-onset progressive cerebellar syndromes.

Keywords: *cerebellar ataxia, (18F)-FDG PET/CT, cerebral glucose metabolism, brain atrophy*

---

1. Introduction

Adult-onset progressive cerebellar disorders can result from many pathological processes, including malformations, degenerations, vascular diseases, infections, neoplasms, paraneoplastic syndromes, toxic/metabolic disorders, and demyelinating disease (1, 14). The diagnosis of degenerative cerebellar diseases is usually based on the medical history, neurological

examinations, laboratory investigations, and presence of cerebellar and brainstem atrophy on Computed tomography scans (CT) and Magnetic resonance imaging (MRI) (2, 6).

In the last decades, nuclear medicine techniques have played a crucial role in the differential diagnosis of various movement disorders. Respectively, single photon emission computed tomography (SPECT) and positron emission tomography (PET) have been used in the diagnosis of patients with acute or chronic genetic and non-genetic ataxias (7). PET scanning is known as a noninvasive imaging method for assessment of cerebral metabolic and neurotransmitter activity, blood flow, as well as neurotransmitter receptor density (9, 11). Evidently, (18F)-FDG PET has improved the detection of etiology and understanding of underlying pathophysiologic mechanisms in progressive non-genetic cerebellar disorders (4, 8, 10, 12). In accordance with the aforementioned data, we studied the cerebral glucose metabolism and neurological dysfunction in seven patients with late-onset cerebellar ataxia.

2. Material and Methods

Seven patients (2 Males and 5 Females, aged between 31 and 59 years) with idiopathic cerebellar ataxia were included in this study. Neurological status examination and additional laboratory investigations were carried out. All patients underwent MRI and (18F)-fluoro-2-deoxy-D-glucose (FDG) PET/CT. FDG activity was calculated based on body weight (0,14mCi/kg) and administered through an intravenous line. Patients were scanned with Phillips Gemini TF (16slice) PET/CT, using the following parameters - Low Dose CT 120keV, 50mAs from vertex to mid-thigh and corresponding PET scan field with 576mm FOV, 4mm pixel size, 10 minutes per frame (Brain PET/CT protocol). Iterative reconstructions of PET raw data were done, following the standard manufacturer's algorithm for Brain CTAC in two image sets: PREVIEW (3D-RAMLA) and Brain CTAC (LOR-RAMLA) with opportunity for fusion with CT scans. The pattern of cerebral glucose metabolism in cerebellar ataxia was compared to the results of healthy controls. Brain magnetic resonance imaging (MRI) was performed using a GE 1.5 T, Signa Excite HDxt system.

3. Results

All the patients experienced onset of their symptoms beyond the age of 30 years. Detailed medical history, physical findings and laboratory investigations excluded other acquired causes of cerebellar ataxia. The main symptoms involved dysarthria, dysmetria and intention tremor in arms, dysdiadochokinesis, and truncal ataxia. CT/MRI data revealed different severity of cerebellar atrophy. (18F)-FDG PET showed decreased metabolic activity in cerebellum and exceptionally in the pontine region or cerebral cortex. Hereby, we illustrate the clinical and neuroimaging findings in two patients, included in the study.

Case 1

A 59 year old woman without previous medical illness was referred for investigation of vertigo, dizziness, dysarthria, and severe gait imbalance with secondary falls towards the left side. The symptoms have developed progressively for the last 4 years. On admission, her blood pressure, pulse rate, and body temperature were normal. She was alert and had a full range of extraocular movements. There was an evoked bilateral horizontal nystagmus on lateral gaze. She had moderate dysarthria, mild bilateral dysmetria and intention tremor in arms, dysdiadochokinesis as well as truncal ataxia. All laboratory analyses, transcranial Doppler ultrasound, and neurocognitive tests were within normal ranges. Findings of central otoneurological syndrome were recorded. Brain CT revealed mild symmetrical cerebellar atrophy (Fig.1). (18F)-FDG PET showed dramatically decreased metabolic activity in cerebellum and mild - in both parietal regions (Fig. 2).

Figure 1 Brain CT reveals mild symmetrical cerebellar atrophy.

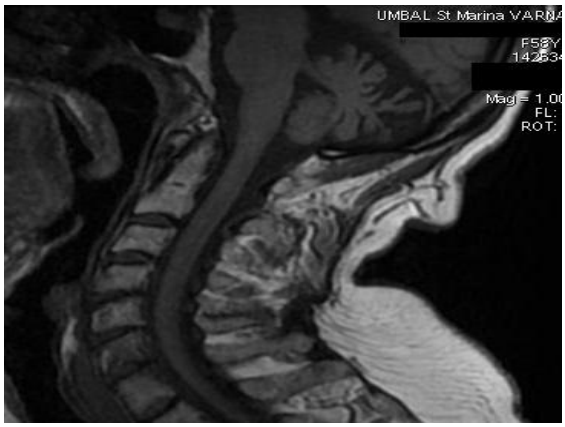
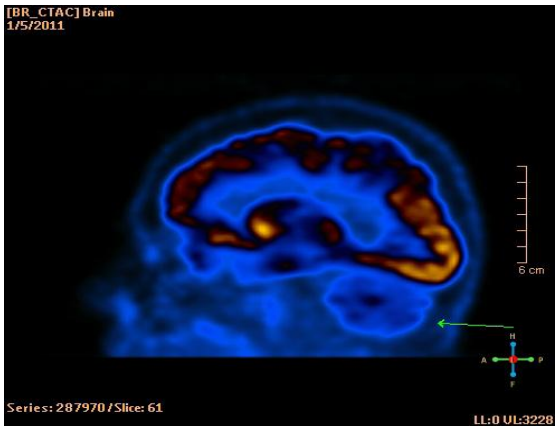


Figure 2 (18F)-FDG PET shows severe hypometabolism in cerebellum and mild - in parietal regions.



Case 2

A 54 year old woman without previous medical illness was referred for investigation of vertigo, voice, speech and handwriting disturbance, head, lower jaw and arms tremor, as well as severe gait imbalance with several incidents of falling. The symptoms have been permanent and progressive for the last 3-4 years. Medical history revealed previous thyrotoxicosis and multinodular goitre. On admission, her blood pressure, pulse rate, and body temperature were normal. She was alert and had a full range of extraocular movements. There was bilateral horizontal nystagmus on lateral gaze, worse towards the right side. She had moderate dysarthria, lower extremities weakness, bilateral dysmetria and intention tremor in arms and legs, dysdiadochokinesis (all worse on the left side) as well as broad-based ataxic gait. All laboratory analyses, including toxic elements exposure, autoantibodies evaluation, neuroinfections, and evaluation of endocrine function were within normal ranges. Transcranial Doppler ultrasound demonstrated no clinically significant cerebrovascular abnormalities. Neurogenetic and neurocognitive tests (MMSE) were normal. Brain MRI revealed severe cerebellar (both hemispheres and vermis) and distal pontine atrophy (Fig. 3). (18F)-FDG PET showed dramatically reduced metabolic activity in cerebellar hemispheres, vermis, and pons (Fig. 4).

Figure 3 MRI shows cerebellar and pontine atrophy.

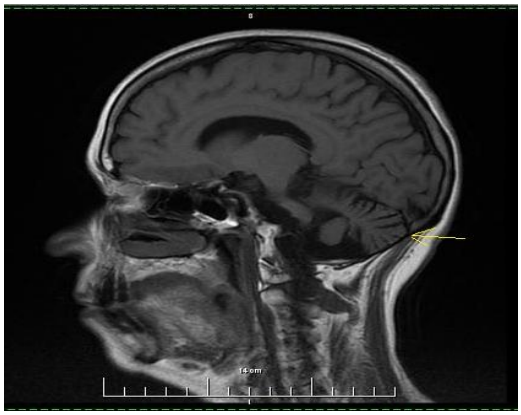
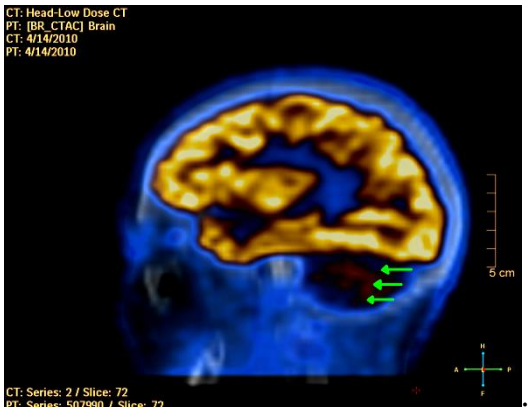


Figure 4 (18F)-FDG PET reveals dramatically reduced radiotracer uptake in the cerebellum.



4. Discussion

In this study, we present clinical and neuroimaging data of seven patients with manifestations of progressive cerebellar disorder. The age at symptoms onset of all patients was over 30 years. Neurological examinations revealed similar to previously described by Abele M, et al (1) clinical features of ataxia that corresponded to cerebellar impairment. Therefore, the final diagnosis of late-onset cerebellar ataxia was considered in all our cases.

Cerebellar dysfunction may result from various genetic and non-genetic causes, e.g. neurodegenerative idiopathic late onset cerebellar ataxia (3, 5, 13). In this study, detailed medical history, physical findings and laboratory investigations excluded other acquired causes of cerebellar ataxia, such as vascular, neoplastic, paraneoplastic, inflammatory, toxic, etc.

According to the literature, CT scans and MRI show evidence of cerebellar and sometimes brainstem atrophy in approximately 50% of patients (2, 6). In this context, our structural brain scans demonstrated cerebellar atrophy in all patients and found no evidence for other structural lesions. Respectively, we supposed a diagnosis of idiopatic neurodegenerative cerebellar ataxia.

In the last decades, a large number of PET studies in patients with ataxia have revealed a dramatic reduction of glucose metabolism in cerebellar hemispheres, vermis, brainstem, and dentate nuclei (3, 8, 10, 12). In addition to aforementioned anatomical imaging results, we performed further functional brain scanning with (18F)-FDG PET. Our findings of moderate to severe cerebellar and brainstem hypometabolism were in correspondence with previously published results by Gilman, S. (5), Otzuka, M. (9), and Worth, P. (14). In two patients, we also found a significant reduction in absolute values of regional glucose metabolism in the cerebral cortex. Wang, P. et al (13) showed similar variable patterns of sub- and supratentorial glucose metabolism in individuals with hereditary ataxias.

5. Conclusion

In the present study, (18F)-FDG PET showed abnormal patterns of glucose metabolism that corresponded to the picture of cerebellar impairment. Furthermore, this non-invasive diagnostic technique succeeded to document the influence of cerebellar disease on supratentorial neuronal function with relative sparing of the cerebral cortex. Based on our own clinical and neuroimaging findings, we supported the notion that brain FDG PET scanning may be useful as a complimentary diagnostic tool in evaluation of patients with adult-onset chronic cerebellar syndromes.

References

1. ABELE, M., BURK, K., SCHOLS, L. ET AL. The aetiology of sporadic adult-onset ataxia. Brain. 2002, vol. 125, pp. 961-968.

2. BANG, O., LEE, P., KIM, S. ET AL Pontine atrophy precedes cerebellar degeneration in spinocerebellar ataxia 7: MRI-based volumetric analysis. Journal of Neurology, Neurosurgery & Psychiatry. 2004, vol. 75, pp. 1452-1456.

3. CHAUDHRY, M., GOK, B., WAHL, R. Brain 18F-FDG PET/CT findings in patients with possible paraneoplastic syndrome. The Journal of Nuclear Medicine. 2011, vol. 52, p. 1218.

4. FELLGIEBEL, A., SIESSMEIER, T., WINTERER, G., ET AL. Increased cerebellar PET glucose metabolism corresponds to ataxia in Wernicke-Korsakoff syndrome. Alcohol. 2004, vol. 39, pp. 150-153.

5. GILMAN, S., MARKEL, D., KOEPPE, R., ET AL. Cerebellar and brainstem hypometabolism in olivopontocerebellar atrophy detected with positron emission tomography. Neurology. 1988, vol. 23, no. 3, pp. 223-230.

6. KUCHLING, J., SINNECKER, T., BOZIN, I., ET AL. Ultrahigh field MRI in context of neurological diseases. Nervenarzt, 2014, vol. 85, no 4, pp. 445-58.

7. MISHINA, M. Positron emission tomography for brain research. Journal of Nippon Medical School, 2008, vol. 75, no, 2, pp. 68-76.

8. MISHINA, M., SENDA, M., OHYAMA, M., ET AL. Regional cerebral glucose metabolism associated with ataxic gait - an FDG-PET activation study in patients with olivopontocerebellar atrophy. Rinsho Shinkeigaku. 1995, vol. 35, no. 11, pp. 1199-1204.

9. OTSUKA, M., ICHIYA, Y., KUWABARA, Y., ET AL. Striatal 18F-dopa uptake and brain glucose metabolism by PET in patients with syndrome of progressive ataxia. Journal of Neurological Sciences. 1994, vol. 124, no. 2, pp. 198-203.

10. RENARD, D., COLLOMBIER, L., CASTELNOVO, G., ET AL. Radiation therapy-related ataxia associated with FDG-PET cerebellar hypometabolism. Acta Neurologica Belgica. 2010, vol. 110, no. 1, pp.100-102.

11. SINGHAL, T. Positron emission tomography applications in clinical neurology. Seminars in Neurology, 2012, vol. 32, no 4, pp. 421-31.

12. YOUNES-MHENNI, S., JANIER, M., CINOTTI, L., ET AL. FDG-PET improves tumour detection in patients with paraneoplastic neurological syndromes. Brain. 2004, vol. 127, pp. 2331-2338.

13. WANG, P., LIU, R., YANG, B., SOONG, B. Regional patterns of cerebral glucose metabolism in spinocerebellar ataxia type 2, 3 and 6: a voxel-based FDG-positron emission tomography analysis. Journal of Neurology. 2007, vol. 254, no. 7, pp. 838-845.

14. WORTH, P. Sorting out ataxia in adults. Practical Neurology. 2004, vol. 4, no. 3, pp. 130-151.