

Alexia with Agraphia Following Cerebral Venous Thrombosis Associated with Oral Contraceptive Use

Mohammad Amin Farzi^{*}, Rikhtegar R and Hasaneh S Tamar

Neurosciences Research Center, Imam Reza Medical Center, Tabriz University of Medical Sciences, Iran

^{*}Corresponding author: Mohammad Amin Farzi, Neurology Resident, Neurosciences Research Center (NSRC), Imam Reza Medical Center, Tabriz University of Medical Sciences, Iran, Tel: +98 41 33341249; E-mail: farzi.neuro@gmail.com

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Abstract

Alexia with agraphia is a rare language disorder, which is mostly caused by a stroke in the territory of the middle cerebral artery, with infarction of the inferior parietal lobule that mostly caused by arterial ischemic infarct and venous infarction associated with cerebral venous thrombosis has not been mentioned as a etiology for this disorder and this is the first case presenting by this etiology yet published in literature.

Keywords: Alexia with agraphia; Cerebral venous thrombosis; Oral contraceptive

Case Report

A 26-year-old right handed female was admitted to hospital after few days of severe headache following 10 days of oral contraceptive use. She had never experienced such headaches. Headaches were generalized none throbbing and sometimes was associated with nausea and vomiting. Her past medical history was insignificant other than oral contraceptive usage for 10 days. Her physical examination was normal.

The neurological examination revealed right homonymous hemianopia. The visual acuities were normal on both sides with grade 1 papilledema. In the language examination, her speech was fluent and comprehensive with normal repetition but impaired writing reading naming and calculation (Boston Diagnostic Aphasia Examination). These clinical features were consistent with alexia with agraphia. The remainder of the examination was unrevealing. Her complete blood count showed Hb levels 11 mg/dl. Leukocyte and platelet counts were normal.

The rest of the blood biochemistry was normal. Immunologic tests including antinuclear antibody, ANCA, anti Ro, anti La antibodies, anti-dsDNA, anticardiolipin IgM and anticardiolipin IgG levels did not reveal any pathology. The activated partial thromboplastin time, prothrombin time were within normal limits. Protein C and protein S concentrations measured by an automated functional clotting assay for the quantitative determination of protein C and protein S in human, respectively. Antithrombin III level was normal. Factor V Leiden mutation was negative. Cranial computed tomography (CT) without contrast performed on the day of admission showed hyperdensity of the left sigmoid sinus associated with a left inferior parietal hyper density (Figure 1). Magnetic resonance imaging (MRI) revealed a left parietal lobe lesion with both hypointense and hyperintense components on T1 and T2 weighted images consistent with a haemorrhagic infarction (Figure 2a).

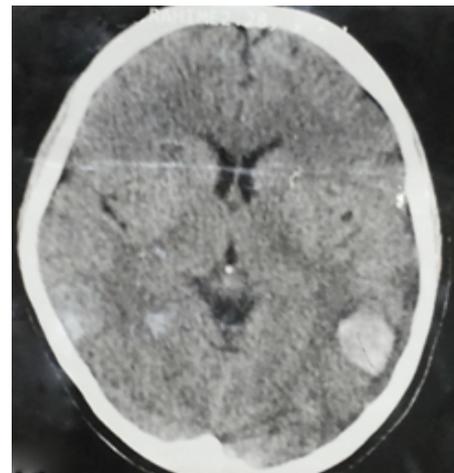


Figure 1: Non-contrast CT scans showing hyperdense focus in left inferior parietal lobule.

Magnetic resonance angiography (MRA) revealed thrombosis of the left transverse and sigmoid sinuses (Figure 2b). She was treated with intravenous heparin continued with oral warfarin with target INR of 2.0-3.0. On the sixth day of admission, she was yet unable to read and write but there was some improvement in naming and calculating. When she left the hospital at the end of 2 weeks, she was still continuing alexia and agraphia with subtle improvement. On follow up visit 2 weeks after discharge there was complete recovery of his symptoms.

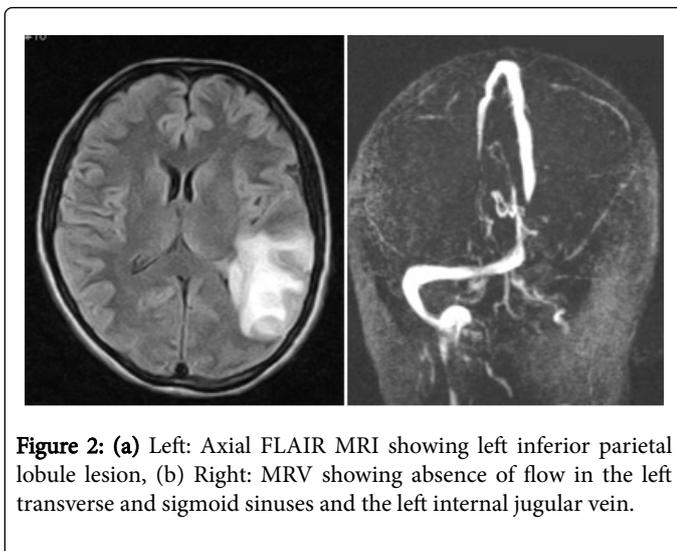


Figure 2: (a) Left: Axial FLAIR MRI showing left inferior parietal lobule lesion, (b) Right: MRV showing absence of flow in the left transverse and sigmoid sinuses and the left internal jugular vein.

Discussion

Alexia with agraphia was first described by French neurologist Dejerine in 1892 in a patient with infarction of the dominant angular gyrus and subjacent white matter and the syndrome has since been well-documented in patients with vascular or neoplastic lesions [1-3].

Synonyms for this syndrome include parietal-temporal alexia, angular alexia, central alexia, and semantic alexia [4] in this type of aphasia reading and writing are both disrupted with writing impairment usually equal in severity to the alexia, and without significant dysfunction of other language modalities [5]. However pure type of this aphasia (as our patient) is rare and this disorder often overlaps with Wernicke's aphasia. In those cases, the patients often have a paraphasic output, impaired naming, and poor repetition, as well as disturbed written comprehension (word blindness) more than auditory comprehension (word deafness).

On the other hand Alexia with agraphia in the pure form can be named acquired illiteracy, with intact spoken language modalities. The syndrome is associated with focal lesions of the left angular gyrus and has anatomopathologic correlation with Gerstmann syndrome. There are some reports of this syndrome by lesions of left posterior inferior temporal and thalamus [6] and even as a presentation of seizure [7].

Gerstmann's syndrome includes agraphia, inability to calculate, right-left confusion, and finger agnosia, an inability to name or point to specific fingers on the patient's or examiner's hand. Patients display difficulty in comprehending written material that is read silently as well as on reading aloud. Reading of letters and words is impaired, and this difficulty extends to comprehension of numbers and musical notations. The problem with letter identification is not restricted to the visual modality; patients also have problems recognizing words when they are spelled aloud.

Other Associated deficits include a right hemianopia or right upper quadrant defects in nearly all patients. There is usually no hemiparesis or sensory loss but a short-term memory deficit may be seen due to the damage of the medial temporal lobe.

Cerebral venous thrombosis (CVT) accounts for less than 1% of all strokes [8]. The disease occurs in all age groups with peak incidences in neonates and in adults in their third decade with a female/male ratio

of 1.5-5 [9]. The presenting clinical picture depends on the extension, localization and activity of the thrombotic process as well as on the presence of venous collaterals [10]. Headache is the most frequent symptom of CVT and occurs in 95% of all cases [8]. In most cases, headache precedes the development of other neurological deficits for days. Focal neurological signs are the most common finding. They include central motor and sensory deficits, aphasia or hemianopia and occur 40% to 60% of all cases. Our patient had a history of occipital head pain for 10 days when she was admitted in hospital with alexia with agraphia, found on neurological examination. As mentioned earlier the usual lesion for this disorder is one that destroys the angular gyrus in inferior parietal lobule. That was the case in our patient that lesion was restricted to the left inferior parietal lobule and alexia with agraphia was a transient disorder.

The diagnosis of CVT is based on neuroimaging. CT is usually the first investigation performed in the emergency room. The cord sign, a visualization of a hyperdense thrombosed cortical vein and a dense triangle sign indicating a fresh thrombus in the posterior part of the superior sagittal sinus are direct signs of CVT on unenhanced CT [11,12]. Empty triangle or delta sign, a non-filling of the confluence sinuum on contrast enhanced CT is the most frequently observed direct sign [13]. MRI and MRA are the best tools both for the diagnosis and follow up of CVT [14]. Within the first days, the thrombus appears isointense on T1-weighted and hypointense on T2-weighted images. An absence of flow void in the form of higher intraluminal signal intensity is observed after administration of gadolinium. In the majority of cases multiple small intraparenchymal haemorrhages surrounded by a hypodensity, which is compatible with venous hemorrhagic infarction is found. Pathophysiologically, venous thrombotic occlusion increases venous and capillary pressure and thus promotes diapedesis of erythrocytes causing haemorrhagic infarcts in CVT. MRV shows a loss of signal due to absence of flow-of the thrombosed sinus. Unenhanced CT of our patient showed hyperdensity of the left sigmoid sinus associated with a left inferior parietal hyperdensity (Figure 1). MRI revealed a left inferior parietal lobule lesion with both hypointense and hyperintense components on T1- and T2-weighted images consistent with a hemorrhagic infarction. MRV showed thrombosis of the left transverse, sigmoid sinuses and the left internal jugular vein.

Underlying conditions which may cause CVT are varied. The etiology remains unknown in up to 35% of cases. A hereditary thrombophilia will be found in 20% to 30% of patients. Common inherited thrombophilic dispositions are the factor V Leiden mutation, 20210 G to A mutation of the prothrombin gene, antithrombin, protein C and protein S deficiency. Factor V Leiden mutation is detected in 15% to 17% and prothrombin gene mutation in 10% to 12% of the cases whereas protein C and S deficiency is rare and detected in only 2% to 6% of cases. Several studies have indicated that the combination oral contraceptives and thrombophilia greatly increased the risk of CVT. Nevertheless, in our CVT patients laboratory workup for underlying hypercoagulable state is usually negative and OCP use remains the only underlying cause in most of our patients in Tabriz and all over the Iran [15,16].

Available treatment data from collected trials favour the use of anticoagulation in patients with CVT. However, controlled data about the optimal duration of therapy does not exist. Oral anticoagulation is recommended for 3 months in patients with idiopathic CVT and for 3-6 months if it is related to pregnancy or oral contraceptives. In patients with hereditary thrombophilia it is used for 6-12 months or

longer. Anticoagulant therapy was instituted in our patient after the diagnosis of CVT was verified. Alexia with agraphia showed prominent regression at the end of two weeks.

In the current literature, this is the first case with alexia with agraphia due to CVT associated with oral contraceptive usage.

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