Clinical manifestations and morphological changes in one case with post-stroke Klüver–Bucy syndrome

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Abstract
We present the case of a 71-year-old right-handed male, admitted to the Department of Neurology, Emergency County Hospital of Arad, Romania, on November 2015, with a rare case of Klüver–Bucy syndrome (KBS), following an ischemic stroke of the right temporal lobe, which was previously diagnosed in December 2014 and was treated accordingly. At the moment of second hospital admission, the patient was found somnolent and confused at home, with traumatic signs of biting of the tongue and urine emission. A couple days after admission, our patient became alert and presented hypersexuality, hypermetamorphosis, increased oral tendency, behavior changes including apathy with loss of anger and fear, and a very increased appetite, transient visual agnosia and right-left disorientation. In the initial phase, the patient could not recognize any members of his family, but he had a tendency to touch everything within his reach and place it into his mouth. The KBS presented in this case, following an ischemic stroke of the right temporal lobe provides distinct and intriguing insights into the possible pathophysiology of this syndrome. Often disruption of consciousness during recovery period may hide the clinical manifestation of the syndrome.

Keywords: Klüver–Bucy syndrome, hypersexuality, hyperorality, visual agnosia, temporal stroke.

Introduction
The Klüver–Bucy syndrome (KBS) is a neurobehavioral syndrome and can be found in relationship with a multitude of neurological disorders. The first case of KBS was observed in a 22-year-old male patient, whom presented herpes simplex meningoencephalitis, which determined bilateral temporal lobe damage [1]. The main symptoms of KBS first described by Klüver and Bucy after an experimental model produced by removal of temporal lobes in Rhesus monkeys [2] include the following: oral tendency (the patients introduce in their mouth different objects), visual agnosia, behavior changes such as lack of any emotional response, apathy, hypersexuality, hypermetamorphosis, and also changes of dietary habits. Even though some clinical features of KBS are identical in humans and Rhesus monkeys, there are some indications that other manifestations like amnesia, aphasia, and seizures are present only at humans [3].

Extremely often, the KBS is incorrectly diagnosed and sometimes not recognized at all, being associated with a psychiatric disorder. Therefore, patients with the clinical manifestations of this syndrome, whom are misdiagnosed with depression or psychoses are treated with psychiatric medications which can interfere with normal brain recovery [4].

Several studies shown that unilateral or bilateral lesions of the temporal lobes, lesions of the amygdala or the frontal cortex can determine symptoms of the KBS, but in most of the presented cases were reported only partial symptomatology [5]. Even tough symptoms of the KBS can be present in a variety of neurological pathologies such as viral encephalitis, stroke, epilepsy and Alzheimer’s disease, very little is known about the treatment of the KBS. Different studies describe that Carbamazepine alone, or a combination of antipsychotics and Carbamazepine can be sometimes effective [6, 7].

The purpose of this article is to present a case of partial Klüver–Bucy syndrome following an ischemic stroke located on the right temporal lobe, in which the morphopathological aspects of the temporal lobe and limbic area were presented at the postmortem examination.

Case presentation
A 71-year-old right-handed man, smoker (two packs a day) was admitted to the Department of Neurology, Emergency County Hospital of Arad, Romania, in October 2014, with ischemic stroke with the following symptoms: disturbance of consciousness, left hemiparesis of the hemibody and left visual field deficit. A computed tomography (CT) scan was performed at admission (CT 520 Series General Electric Optima SYS) and revealed an ischemic stroke of the temporal lobe, with surrounding diffuse brain...
edema, due to the occlusion of the right middle cerebral artery. Also, the thalamus and amygdala were affected by the ischemic lesion (Figures 1 and 2). Moreover, there were performed work-ups for the coagulation profile, autoimmune diseases, vasculopathy, hemoleucogram and biochemistries. During hospitalization, the patient was treated with Cerebrolysin, depletive medication (Furosemide), beta-blockers, statin and anti-coagulant (Clexane). Ten days after the event, the patient was released from Hospital, conscious and cooperative, still recovering the motor deficit. Antiplatelet drug was prescribed for secondary stroke prevention. At the three-month check-up, the patient presented left sequelae motor deficit, and was walking using unilateral help, and left visual field deficit.

In November 2015, he was found somnolent and confused at home, with traumatic signs of biting of the tongue and urine emission. A neurological examination performed at admission to Hospital revealed negative meningeal signs, intact cranial nerves function, sequelar left hemiparesis and left positive Babinsky reflex, and no response to visual stimulation without eye contact. A couple days after admission, our patient became alert and presented hypersexuality, hypermetamorphosis, increased oral tendency, behavior changes including apathy with loss of anger and fear, and a very increased appetite, transient visual agnosia and right-left disorientation. In the initial phase, the patient could not recognize any members of his family, but he had a tendency to touch everything within his reach and place it into his mouth. He tried to hug and kiss female medical staff, became quickly distracted and showed little emotions. When became very agitated, the patient had to be restrained, but calmed down really fast when his attention was distracted. The electroencephalography performed revealed on the temporal area diffuse slow waves. Initially, the patient was treated with Phenytin (50 mg/mL) 5 mL/day and Valium 10 mg/day, but became more hypersexual. The medication was discontinued and Haloperidol was introduced to control the agitation episodes and behavior modification, and also 300 mg of Timonil retard twice a day. Six months later, the patient still had hyperorality and appetite disturbances, but present less hypersexuality.

Unfortunately, at the end of 2016, the patient was involved in a car accident and deceased. A full autopsy was performed, and a sample for the histopathological examination was collected from the right fronto-temporal and occipital lobe. The macroscopic examination realized on fragment with dimensions of 4/3/2.5 cm showed a firm consistency, whitish gray with black dots in color, and blackish leptomeninges (Figure 3).

For the histopathological and immunohistochemical study, we harvested brain fragments both from the stroke area and from the counter-lateral hemisphere, subsequently being fixed in 10% neutral formalin and included in paraffin, according to the usual histopathological protocol. The histopathological study was performed on samples stained with Hematoxylin–Eosin (HE), and for the histological study, we used the following antibodies: anti-CD34, QBEnd10 clone, Dako, 1/50 dilution; anti-GFAP (glial fibrillary acidic protein), 6F2 clone, Dako, 1/200 dilution; anti-NeuN (neuronal nuclei) polyclonal, Abcam, 1/100 dilution.

The histopathological examination from the stroke area showed a widening of the luminal caliber of the leptomeningeal vessels, with numerous red blood cells and few leukocytes. In the leptomeninges, there were observed extravasated red blood cells, amorphous eosinophilic deposits and leukocyte polymorphous moderate infiltration. Also, numerous red blood cells and some leukocytes can be observed inside the cerebral vessels lumen, and an area where brain matter appears disorganized and presents itself as an intensely eosinophilic material with “areolar” aspect, with glial cells, macrophages with intracytoplasmic dark brown pigment, some plasmocytes, lymphocytes and little free pigment. The remaining neurons presented intense eosinophilic and homogeneous cytoplasm, pyknotic or missing nuclei.

The histopathological study from the counter-lateral hemisphere showed a significant reduction of the neuronal density, especially in the superficial layers of the brain cortex, which presented a spongy aspect due to neuron death, with a moderate perivascular and perineuronal edema (Figure 4), brain microhemorrhages, with the perivascular extravasation of red blood cells in the Virchow–Robin space (Figure 5) and moderate vascular congestion in the arterioles and venules of the white matter (Figure 6).
Anti-CD34 antibody immunomarking highlighted a reduction of the microvascular density in the cortex, associated with frequent vascular discontinuities that explain the presence of microhemorrhage infiltrates (Figure 7), the anti-NeuN antibody immunomarking showed a low reactivity, thus showing a chronic suffering (Figure 8), and the marking of astrocytes with the anti-GFAP antibody showed extended areas of brain gliosis (Figure 9). The final diagnosis was an ischemic stroke of the right temporal lobe, thalamus and amygdala.

Figure 4 – Macroscopic image from the superficial layers of the brain cortex with a spongy aspect because of the neuronal apoptosis, associated with a moderate perivascular and perineuronal edema. HE staining, ×200.

Figure 5 – Perivascular brain hemorrhage in the Virchow–Robin space. HE staining, ×400.

Figure 6 – Vascular congestion in the white matter. HE staining, ×200.

Figure 7 – Image from grey matter where there can be observed the reduction of blood capillaries number. Anti-CD34 antibody immunomarking, ×200.

Figure 8 – Neurons from the cortex with a low reactivity to NeuN. Anti-NeuN antibody immunomarking, ×200.

Figure 9 – Area of white matter with intense reactive gliosis. Anti-GFAP antibody immunomarking, ×400.
Study, Formisano temporal lobes, thalamus and amygdala, structures that receive projections from the Klüver–Bucy patients is due to the loss of cortical function. The increase of the sexual libido of the patients is determined by lesions of the temporal lobes similar to cases of Klüver–Bucy syndrome. The hypersexuality, contrasting with the emotional behavior, was observed in this case. The oral tendency to place objects into the mouth. The changes of sexual behavior were reflected by impulse to grab any objects in sight and put it into the mouth. The changes of sexual behavior were reflected by impulse to grab any objects in sight and put it into the mouth. The changes of sexual behavior were reflected by impulse to grab any objects in sight and put it into the mouth.

A study performed by Pilleri showed that oral grasping is determined by lesions of the temporal lobe similar to cases of Klüver–Bucy syndrome. The hypermetamorphosis of our patient, with the hand grasping determined by the lesions of the frontal lobe [16]. The hypermetamorphosis of our patient, defined as attraction for visual stimuli, consisted of an impulse to grab any objects in sight and put it into the mouth. The changes of sexual behavior were reflected by hypersexuality, contrasting with the emotional behavior, in this case the patient being very calm and with no emotional reactions. In previous studies, there was suggested that the increase of the sexual libido of the Klüver–Bucy patients is due to the loss of cortical inhibition over the limbic system [17]. The frontal cortex and the limbic system receive projections from the temporal lobes, thalamus and amygdala, structures that are associated with memory and emotions. In a previous study, Formisano et al. states that the appearance of the KBS can be associated with a good prognosis in the outcome of cerebral lesions with loss of consciousness [18].

From the anatomical standpoint, the Klüver–Bucy syndrome follows bilateral malfunctions of the temporal lobes, but also the amygdala, uncus, hippocampus and cingulated gyrus have an important role in the pathogenesis of this syndrome. The disruption of neurological pathways, which connect the frontal lobe, limbic system and medial thalami responsible for memory and emotions, can also produce the KBS [19, 20]. On the other hand, symptoms of KBS were described after unilateral lesions, such as subdural right hematoma or lobectomy of the left temporal lobe. In their studies, Geschwind described the syndrome as a result of disruption of visual input to limbic system [21–24], and Müller et al. viewed a KBS appearing after destruction of the pathways connecting the frontal cortex, limbic area and thalamus [14, 25]. However, in our case, the ischemic stroke was located at the right temporal area, amygdala and mesial temporal area. Often disruption of consciousness during recovery period may hide the clinical manifestation of the syndrome. Despite the fact, the CT scan is a distinctive imaging method for patients who suffer brain injuries; in those with neurobehavioral changes, we must perform a magnetic resonance imaging (MRI) to visualize the structural brain lesions [19, 24, 26]. To be noted that the clinical symptoms of KBS appear not only in patients with morphological lacerations of the temporal areas visible on CT scan, so this very rare syndrome should be taken into account at different patients whom sustained severe cerebral accidents.

The clinical outcome of KBS is different from one patient to another, and it is reversible in patients with infections, traumatic injuries or seizures if it is diagnosed as soon as possible and treated accordingly. The treatment of KBS may be a challenge, some patients having great results when treated with antiepileptics, such as Carbamazepine, or Haloperidol, but in others, there was observed the persistence of the mental disorders or the development of a Korsakow syndrome [25, 26].

**Discussion**

To the best of our insight, this is the first case presented in Romania of a KBS following a unilateral ischemic stroke of a temporal lobe. Any combination of three or more clinical manifestations is very suggestive for a KBS. In humans, a complete KBS is extremely rare [8–10], more often being incomplete [7, 11, 12]. Even though the presence of the KBS was shown following bilateral lesions of the temporal lobe, there are a few studies that report the syndrome without bitemporal lesions [13–15].

There should be noted that a transitory dysfunction of the temporal lobes can be determined by epileptic or hemodynamic incidents.

In our case, the most important clinical manifestations observed in our patient were the changes of the sexual behavior, apathy, hypermetamorphosis, altered dietary habits and the oral tendency to place into his mouth all surrounding objects including sharp or inedible objects, so a number of five major symptoms of KBS as presented by Rossitch & Oakes in a previous study [15]. Sometimes, during hospitalization, the patient movements were extremely compulsive, so in those moments the patient had to be restrained. In our particular case, the oral tendency was not a combination of grasping with the mouth and the hands, the hands were used only as help. A study performed by Pilleri showed that oral grasping is determined by lesions of the temporal lobe similar with the hand grasping determined by the lesions of the frontal lobe [16]. The hypermetamorphosis of our patient, defined as attraction for visual stimuli, consisted of an impulse to grab any objects in sight and put it into the mouth.

The changes of sexual behavior were reflected by hypersexuality, contrasting with the emotional behavior, in this case the patient being very calm and with no emotional reactions. In previous studies, there was suggested that the increase of the sexual libido of the Klüver–Bucy patients is due to the loss of cortical inhibition over the limbic system [17]. The frontal cortex and the limbic system receive projections from the temporal lobes, thalamus and amygdala, structures that are associated with memory and emotions. In a previous study, Formisano et al. states that the appearance of the KBS can be associated with a good prognosis in the outcome of cerebral lesions with loss of consciousness [18].

Conflict of interests

The authors state that they have no conflict of interests.

**References**

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