

# **RESEARCH ARTICLE**

#### **RECURRENT ISCHEMIC STROKE IN A CANNABIS USER UNDER 30: A CASE REPORT**

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# Manuscript Info Abstract

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*Key words:-*Ischemic Stroke, Recurrent Stroke, Cannabis Use Cerebrovascular disease is one of the overlooked complications of cannabis use. In young patients presenting with symptoms of ischemic stroke, the recent use of cannabinoids should be systematically investigated. Yet, cannabis use is widespread and some countries have taken further steps to legalize it. Here we present the case of a 29-year-old patient who had two several ischemic strokes within two months, each time after an important cannabis ingestion. This case illustrates the role cannabis can play in ischemic strokes occurring in young patients even though the pathophysiology of such an implication is not totally elucidated.

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#### Introduction:-

The incidence of ischemic stroke (IS) has increased in young adults over the past 30 years [1]. The etiologies are many and varied. Up to 50% of strokes have no potential cause [2] whereas the toxic origin is reported in 9 to 12% of young adults IS [3]. Several studies found that drug abusers had an increased risk (6.5 times) of both hemorrhagic and ischemic stroke [4]. Amphetamines and Cocaine are more commonly associated to IS in young adults than opioids and cannabis [5].

Cultivated hemp (Cannabis Sativa) is the most widely consumed drug in the world [6]. Cannabis use is particularly widespread among adolescents and young adults [7]. Yet, the involvement of cannabis in IS among the young has been little studied[8]. According to a report published by the International Narcotics Control Board (INCB) in 2018, Morocco ranks among the first countries producing cannabis resin [9]. Regarding socio-cultural aspects, cannabis is accessible and relatively tolerated in Morocco [10].

Cannabis- related IS may result in functional impotence and loss of autonomy among young patients, with sometimes long and partial recovery [11-12].Considering the recent legalization of cannabis consumption in some countries, research is still needed for a better understanding of cannabinoids potential risks. Here we present the case of a Moroccan young cannabis user who experienced two successive cannabis-related IS within a period of two months.

#### **Case Report**

A 29-year-old male right-handed patient with a twelve years history of regular use of cannabis (5 joints / day) and tobacco (10 cigarettes/ day) presented to the emergency room with acute-onset weakness of the left hemibody. The

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patient had norotherknown vascular risk factors neither medical history. He denied the recent use of psychoactive substance. According to his relatives, symptomatology started within 24 hours following a massive consumption of cannabis.

At admission, the neurologic evaluation found a pyramidal syndrome with hemiparesis. The rest of the somatic examination showed no abnormality. Braincomputed tomography (CT-scan) revealed an infarct in the territory of the right deep middle cerebral artery. Brain magnetic resonance angiography (MRA) corroborated the diagnosis of artery stenosis corresponding to the patient's deficit (figures 1 and 2).

Urine toxicology screening was positive to cannabis and negative to cocaine, amphetamines and opioids. The rest of blood tests (blood count, differential coagulation times, ionogram, serum glucose, creatinine, liver enzymes, C and S Proteins, fibrinogen, d-dimers, C reactive protein, homocysteine, immunological test, HIV, VHB, VHC, and syphilis serology) as well as biochemical and microbiological cerebrospinal fluid examination gave normal or negative results. Electrocardiogram, chest X-ray, supraaortic trunks echography, transthoracic andtransesophagealechocardiographyshowed no anomaly. The patient received aspirin therapy and physiotherapy. He fully recovered within few days, was discharged home and referred to an addiction healthcare service.

Two months later, concomitantly with a massive re-use of cannabis spontaneously reported by the patient, the latter presented with similar symptoms (isolated acute-onset heaviness of the left hemibody). The brain angio-MRI concluded to an ischemiain the territory of the right choroidal artery(figure 3). Exhaustive biological and radiological assessment showed no other anomaly.

The treatment of the patient's second episode consisted of a combination of antiplatelet therapy, fluoxetine and functional rehabilitation. A month after this second admission, the hemiparesis was still persistent. Before the patient was discharged home, he was referred once again to an addiction healthcare service.

### **Discussion:-**

With 181 million users, Cannabis is the most frequent illicit recreational drug used around the world [13,14]. Several cardiovascular complications related to cannabis and synthetic cannabinoids have been reported in the literature [15]. In young adults, ischemic stroke is the most commonly reported adverse neurovascular effect of cannabinoids [16] A study run among patients aged between 18 and 55 and admitted for stroke concluded that cannabis use was independently associated with a 26% increase in the risk of stroke after correction of other known risk factorssuch as obesity, hypertension, smoking and alcohol consumption [17]. Similarly, the US nationwide inpatient sample reported that recreational use of cannabis was independently associated with a 2.25-fold increase in the risk of acute ischemic stroke among people aged 25 to 34 years [18]. Moreover, in a general population survey, Hemachandraand Al. showed that heavy cannabis users have 3.3 times the rate of stroke than non-cannabis users [19].

The most striking about our patient is the recurrence of his IS: two episodes within tow months, each time in the context of cannabis ingestion. Similarly, Matéoet Al. reported the case of a 36-year-old man who had three recurrent strokes over two years, each episode occurring immediately after cannabis consumption [20]. Three recurrences were also reported by Santoset Al. in a 27-year-old patient in the context of cannabis use [21].

In both episodes of IS, our patient had a reversible stenosis that occurred in the anterior vascular territory. One third of the published cases reported multifocal intracranial artery stenosis that turned out to be reversible after the cessation of cannabis use [22,23]. Several theories have been put forward to explain the link between cannabis and ischemic events, including orthostatic hypotension, vasospasm and cardioembolism[24]. In 2010, Ducheneet Al. described the first case associating thromboembolic cerebraland myocardial infarction with massive consumption of cannabis [25]. Farouquiet Al. illustrated the same acute thrombosis mechanism of the left internal carotid artery in a 36-year-oldsynthetic cannabis (K2) user [26]. Cannabis-induced toxic and immune vasculopathy [20,27], cerebralhypoperfusion by peripheral sympathetic effect and vasculitis are also potential mechanisms in cannabis induced IS [3]. Recently, Wolff et Al. demonstrated that cannabis induces mitochondrial respiratory chain dysfunction in rats and increases oxidative stress, which is well known as a mechanism involved in human IS [28,29].

Cannabis use is widespread. Yet, cannabinoids-related neurovascular complications remain rare. One reason is that the implication of cannabis in young adults IS is underestimated. Indeed, in most cases, recent use of cannabis is not investigated nor by questioning neither by laboratory testings[30]. Besides, cannabis-related IS is more likely to occur in users with a genetic predisposition to cannabinoids neurovascular toxicity and with high concentrations of THC in the cannabis ingested [28, 31].

Cannabis ingestion has to be systematically investigated in young adults IS. In the actual context of some countries legalizing cannabis, and others opening up new horizons for its medical use [32], further studies are needed for a better understanding of cannabis potential cerebrovascular risk [8] in order to estimate as precisely as possible the risk/benefit balance. Further research is also needed to unveil pathophysiological mechanisms underlying the role played by cannabinoids in ischemic strokes.

#### Annexes



Figure 1:- Brain Magnetic Resonance Images (MRI) of an axial slice in diffusion sequence showing the IS in the deep right Sylvian territory.



Figure 2:- Brain Magnetic Resonance Images (MRI) of a frontal cut in flair sequence showing the IS in the deep right Sylvian territory.



Figure 3:- Brain Magnetic Resonance Images (MRI) of an axial section in flair sequence showing the 2nd IS in the territory of the anterior choroidal artery.

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