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Case Report

Food-Related Atrial Fibrillation? The Potential Role of Biogenic Amines in "Nutri-Arrhythmias" Genesis

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Abstract: Atrial fibrillation (AF) is the most common type of arrhythmia: a disorganized electrical atrial activity leading to irregular ventricular beats. Its most common risk factors include high blood pressure, congenital and valvular heart diseases, aging, heart failure and coronary heart diseases. Other risk factors include excessive alcohol intake, tobacco smoking, diabetes mellitus and thyrotoxicosis. However, many cases are not associated with any of these risk factors: probably, in these patients, immunological, functional and even dietary mechanisms may be responsible to induce cardiac arrhythmias. Several studies have focused on immunological and neurohumoral mechanisms; however, little information is available about the potential relationship between dietary patterns and atrial fibrillation episodes. This case report describes a potential correlation between biogenic amines in ingested food and recurrent atrial fibrillation onset in a 61-years old man in absence of a remarkable clinical history and of the most common risk factors. The nutritional team instituted a food protocol: a low calories diet and eliminating biogenic amines-rich foods. During the follow-up (16 months), there was a noticeable weight loss and no arrhythmic episodes happened again. This clinical case provides evidence for a possible new relationship between some kinds of food and heart conduction (defining the very novel field of arrhythmogenic foods and of "nutri-arrhythmias"), recognizing biogenic amines-rich foods abuse as the potential trigger and substrate for atrial fibrillation. Therefore, we suggested that clinical history in patients with new onset AF should also include questions concerning the ingestion of histamine-rich foodstuffs (or other amines-rich food) and alcohol consumption: their effects may result to be synergistic in the alteration of cardiac rhythm and may explain the recurrence of an unexplained atrial fibrillation.

Keywords: biogenic amines; vasoactive amines; cardiac arrhythmias; atrial fibrillation; food-related arrhythmias; nutri-arrhythmias

1. Introduction

Heart arrhythmias are a common group of clinical conditions with an abnormal activation of myocardium and a perturbed rhythm of heartbeat. Atrial fibrillation (AF) is the most frequent dysrhythmia, affecting about 4.5 million people across Europe, especially in advanced age [1], with rising incidence/recurrence rates and serious complications. Its occurrence is often related to structural heart alterations, cardiac valve disorders, arterial hypertension, arteriosclerosis or coronary heart

disease [2]. However, a large number of AF occurs in absence of known structural anomalies or cardiovascular diseases and no pathological cardiac findings can be documented [3]. It is unclear whether immunological, infectious or allergic diseases may also be related to AF [4]: probably, in these patients, functional, neurohumoral and even dietary mechanisms may be responsible to induce AF. On the one hand, there is a well-known positive correlation between AF and obesity, inflammation, heavy alcohol consumption, hypertension, type 2 diabetes mellitus and dyslipidemia [5]. On the other hand, there is evidence for a beneficial effect of certain foods such as olive oil, nuts, fish, fruits, vegetables, fiber and whole grains on cardiovascular health. The role of other foods, such as chocolate, is less clear: some studies have demonstrated a beneficial effect of chocolate consumption because of the polyphenols content [6] on several cardiovascular risk factors, including hypertension and heart failure [7]. However, little is known about the association between ingested food and incident AF.

Biogenic amines (BA), such as histamine, tyramine, putrescine, cadaverine, spermine, spermidine, tryptamine, phenylethylamine and octopamine, are biologically active compounds formed through natural biochemical processes taking place at a cellular level [8]. Some BA (such as spermine and spermidine) are accountable for the regulation of cell growth/division and neural transmission; BA are also identified as potential precursors of carcinogenic N-nitroso compounds [9]. Endogenous BA can be present in both fermented and non-fermented food; a high BA concentration is observed in food with high protein content, in particular fermented and ripened food [10].

This is attributable to the higher microbial decarboxylases activity in bacteria, representing the contaminating microflora or intentionally added [11]. However, if their food levels reach a critical threshold, BA may be dangerous to human health [12]. BA-related adverse reactions caused by food ingestion are mainly classified as pseudo-allergies [13]. For example, consumption of food containing high amount of tyramine can cause dietary-migraines in sensitive subjects [12]. High doses of histamine (a most common cause of food poisoning) are associated with a wide variety of physiopathological syndromes [14].

Currently, the only BA whose maximum limits have been set in the EU and the USA is histamine. European legislation (Commission Regulation EC 2073/2005) limits histamine levels to 200 mg kg^{-1} in fresh fish and up to 400 mg kg^{-1} for cured fishery products [15]. The Food and Drug Administration in the USA considers histamine level higher than 500 mg kg^{-1} to be a danger to health [16], with a dose [12] of 50 mg/meal/person histamine NOAEL (no-observed-adverse-effect-level). Considering amine-related risks, many risk assessments about BA occurrence in food, not only in fishery products and fermented cheeses [17], but also in ready-to-eat baby food [18], were performed. The results of amine analysis in baby foods indicated the presence of food ingredients whose amount should possibly be reduced (tuna, beef, spinach, green peas, banana), because of their higher tyramine and putrescine levels which may determine symptoms in children too [18].

After ingestion, oxidation is the main route of BA detoxification, although methylation and acetylation have also been implicated in the detoxification of histamine [19].

Detoxifying oxidation is carried out by specific amine oxidases. These enzymes are usually classified as monoamine oxidases (MAO) and diamine oxidases (DAO), depending on the number of amino groups preferentially oxidized. These oxidases are present in the mitochondria of animal tissues, mainly in liver, kidney, pancreas, intestine, brain and blood [19].

2. Case Presentation

A 61-years old man, ex-factory worker (at present retired) with an unremarkable clinical history presented to the emergency room complaining of palpitations and short breath. He described his heartbeat as irregular and stronger than usual, with a feeling of "the heart beating in the throat". These symptoms occurred in connection with chest pain and respiratory distress, with stomach upset, sweating and feeling of anxiety and trepidation. His familiar anamnesis was negative for lone AF and any cardiovascular diseases. His pathological anamnesis revealed shorter and lighter but quite similar episodes during the previous 10 months, which were spontaneously reversible in

few seconds: probably some sporadic and harmless extrasystoles, perceived as missed or additional heartbeats, which used to occur three/four times per week, especially in post-prandial time (from 15 to 60 min after the meal) and during the weekends. However, the patient did not manage to find any association with a specific kind of food; in addition, he was not able to determine substantial dietary modifications during the previous 10 months, compared to the antecedent period. Upon admission, he denied either consumption of any recreational drugs or new introduction of medication. Moreover, he denied previous fever, vomiting and diarrhea. Physical examination revealed agitation, tachypnea and tachycardia of 150 beats/min. Oxygen saturation (98%) and body temperature (36.8 °C) were normal. Laboratory findings included hyperglycemia (225 mg/dL). Other serum parameters, including complete blood count, electrolytes, renal, thyroid and liver function tests were within normal range. Salicylate blood levels were within normal ranges. Urinary toxicology screen was negative for opiate, amphetamines, methamphetamines and cocaine. A 24-h urine sample was performed in order to investigate the presence of carcinoid syndrome and neuroendocrine/cathecolamine-secreting tumors. The amount of 5-hydroxyindole acetic acid (5-HIAA), which is a breakdown product of 5-hydroxytryptamine, was found to be mildly higher (18 mg/24 h) than the normal range (2–7 mg/24 h or 10.5–36.6 mmol/24 h) [20], even if it was not enough to be suggestive for a neuroendocrine tumor.

In fact, normal urine levels of metanephrine and normetanephrine, as well as accurate imaging techniques, such as computed tomography (CT) scan and magnetic resonance imaging (MRI), excluded any carcinoid lesion, primary tumor and secondary metastasis. The patient denied previous consumption of medicines that could increase 5-HIAA measurements, such as acetaminophene, methocarbamol and reserpine; thus, an interference of ingested food was conjectured. Plain chest X-ray and abdominal X-ray were normal. Electrocardiogram (ECG) demonstrated disorganized atrial rhythm with variable atrioventricular conduction consistent with atrial fibrillation, without evidence of acute myocardial ischemia (Figure 1). AF characteristic findings were the absence of P waves and irregular R–R intervals due to irregular conduction of impulses to the ventricles.

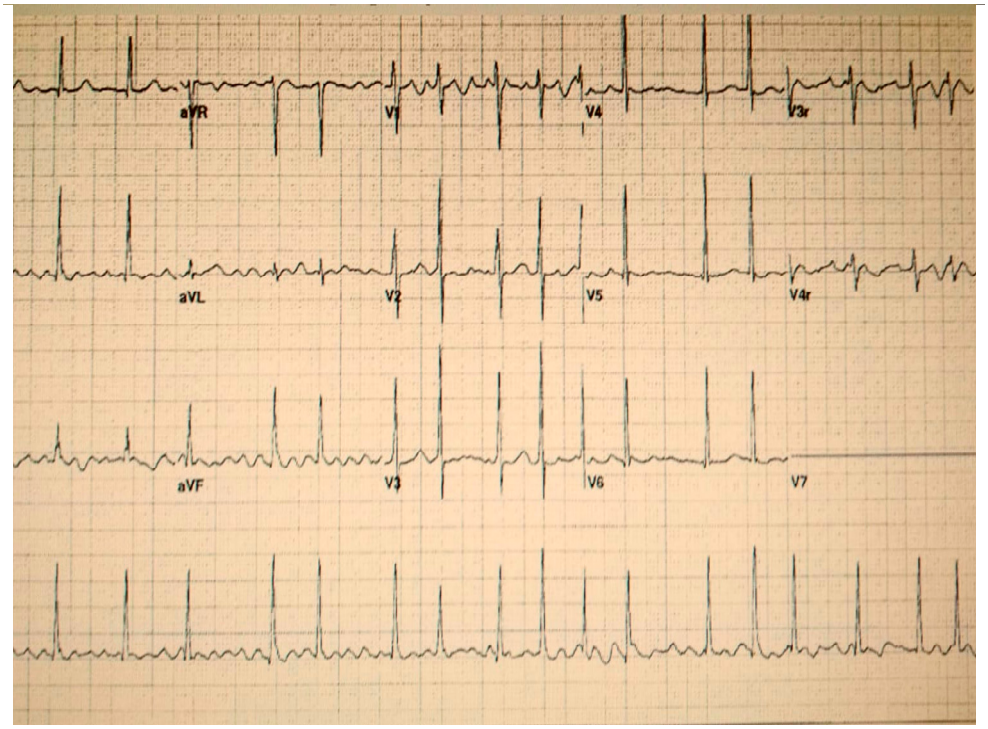

Figure 1. Electrocardiogram (ECG) of the patient upon admission to the Emergency Department demonstrating disorganized atrial rhythm with variable atrioventricular conduction consistent with atrial fibrillation, without evidence of acute myocardial ischemia.

The patient underwent supportive treatment (intravenous fluid administration) and was admitted to the Intensive Care Unit. The cardiologist provided him an anti-arrhythmic treatment (intravenous administration of flecainide acetate 150 mg), which displayed prompt benefits. Within the first day in the Intensive Care Unit, all his complaints resolved, with no needs for further intervention.

After restoring sinus rhythm (which resulted to be stable), a transthoracic echocardiogram was also performed, thus excluding any valvular heart disease, ventricular hypertrophy and pericardial disease. Atrial dimensions resulted to be normal, with an intact interatrial septum; right ventriculum diameters and global diastolic function were also normal, with tricuspid annular plane systolic excursion (TAPSE) >25 mm. The left ventricular ejection fraction, whose dysfunction is usually identified as an independent predictor of ischemic stroke and systemic embolism in AF risk stratification [21], resulted not to be depressed. A mild tricuspid valve incompetence was evidenced. The patient did not undergo transesophageal echocardiogram because his thromboembolic risk was considered to be low.

After 36 h of observation free of symptoms with restored sinus rhythm (Table 1), the patient was discharged home with normal vital signs and glucose level with a diagnosis of "unexplained lone paroxysmal atrial fibrillation". Additionally, he was directed toward a nutritional consult and he underwent an accurate dietary interview. The patient declared he had consumed an excessive amount of dark chocolate (60 g) about 2 h before his admission to the emergency room. He declared to have had lunch three hours before admission: the dietary interview revealed the consumption of some tastes of smoked mackerel (about 100 g) and aged cheese ("Pecorino cheese", about 100 g) as appetizers, white bread (100 g), beef (300 g) with ketchup sauce (25 g), mixed salad (100 g) and fruit salad (made of apple, banana and peach in syrup, about 350 g). Moreover, he had consumed three glasses of red wine (600 mL) as he often used to do. He denied consumption of coffee and energy-drinks in the previous hours and days. Since the subject had widely taken on foodstuffs (known in the literature for the high BAs content) in the same meal, it can be assumed that it had far exceeded the total BA toxic value.

Table 1. ECG parameters during the atrial fibrillation (AF) episode and after stabilization.

Upon Admission to Emergency Room	**Post-AF**
Irregular intervals between heart beats	Restored sinus rhythm
Absence of P waves	Normal P waves
Heart Rate (HR): 150 bpm	Medium HR: 88 bpm
Irregular R-R intervals	Regular conduction of impulses to the ventricles

The actual level of BAs cannot be precisely assessed, because its calculation could only be empirical: we calculated the total amount of BAs in ingested foods (0.09 mg/60 g dark chocolate, 17.1 mg/300 g beef, 130.1 mg/100 g Pecorino cheese, 2.089 mg/100 g smocked mackerel, 0.037 mg/100 g lettuce, 0.308 mg/25 g ketchup sauce, 85.644 mg/600 mL red wine) [22], which resulted to be 235.368 mg. However, this amount is certainly underestimated because of the great variability of BAs concentration, due to many factors: storage conditions, ageing, ripening, brand, etc. In addition, we have not considered some of the BAs because of the lacking literature about them.

Additionally, in the same meal a high content of alcohol was present that inhibits intestinal MAO and increases the intestinal permeability to the already high BA amount [23].

The patient went to our Nutrition Center took in order to improve his nutritional and antropometric profile: he resulted to be a slightly overweight subject, height (H): 174 cm, body weight (BW): 81 kg, body mass index (BMI): 26.75. We investigated any possible connection between food ingestion and his recurrent alteration in cardiac rhythm. The food interview evidenced a large consumption of biogenic amines-rich foods, such as canned fish and meat, ripened cheese and chocolate. In addition, the patient used to drink about five wine glasses per day. Moreover, he revealed the particular postprandial recurrence of cardiologic symptoms such as palpitations; this was also confirmed a week later through the execution of a Holter ECG, evidencing three extrasystoles 30,

50 and 115 min after lunch and two extrasystoles 45 and 60 min after dinner. The mean daily heart rate resulted to be 88 beats/min and the mean nightly heart rate 64 beats/min; the minimum and maximum heart rate recorded were respectively 122 beats/min (at 3.13 pm) and 54 beats/min (at 1.37 a.m.). There were 0 pauses greater than 2.5 s. The nutritional team instituted a food protocol: a low calories diet and eliminating biogenic amines-rich foods and wine (no more than one glass per week). During the follow-up (16 months), there was a noticeable weight loss (−8.4 kg) so that normal weight was achieved (BMI: 23.97) and no arrhythmic episodes happened again.

The cardiologic follow-up confirmed the absence of further problems: after 6 months, another ECG was performed, without evidence of altered cardiac rhythm. After 6 and 12 months, the Holter ECG was repeated, displaying a reduction in extrasystoles: only one event was registered 6 months later (100 min after dinner; however, it was an asymptomatic episode) and no events 12 months later. In addition, the patient self-monitored both blood pressure and resting heart rate daily, displaying no significant measurements.

This study was approved by Department of Medical Oral and Biotechnological Sciences, "G. d'Annunzio" University of Chieti-Pescara (approved date: 2 February 2018). The patient gave his consent to be described in anonymous way in this study: he provided his informed consent verbally for the publication of their information.

3. Discussion

AF shows a high prevalence even in absence of cardiovascular causes. An undefined percentage of AF could be caused by dietetic triggers. Our case report outlines a possible link between AF episodes and some specific foods as trigger factors. Although we have extensive data on diet, lifestyle and comorbidity conditions, we cannot rule out the possibility of residual confounders. Our food frequency questionnaire asked about food intake, defining the frequency of amine-rich foods ingestion; however, we cannot retroactively distinguish the exact amount of ingested biogenic amines. In addition, ECG execution was limited to the case with recorded hospitalization for AF; however, we cannot exclude the incidence of silent AF in the same subject, who had previously often perceived postprandial palpitations. The same association between dietetic triggers and AF episodes was observed by Hansson et al. [24], who conducted interviews with one hundred Swedish subjects who went to the hospital because of a paroxysmal AF. A strict questionnaire investigated any possible trigger, including dietetic factors. Approximately 30% of the patient named alcohol (most of which was represented by red wine); 25% recognized coffee as a trigger; some patients also identified chocolate, nuts and onion as trigger foods. Patton et al. [25] described interviews with 180 serial subjects with AF at a Massachusetts hospital. 34% indicated as a trigger "eating", 16% "eating chocolate", 11% soda, 9% coffee and 4% tea.

3.1. Role of Histamine

Histamine is a vasoactive amine, an organic nitrogenous compound derived from the decarboxylation of the amino acid histidine. It is involved in local immune responses and an immunological mediator in inflammatory conditions, which physiologically regulates some cardiovascular functions and acts as a neurotransmitter. Augmented histamine levels seem to be linked to an arrhythmogenic potential in cellular and animal models: in guinea pigs, a stimulation of the H2-receptor in the right atrium determined an important heart rate acceleration [4].

Stimulation of the H2-receptor in the right atrium and the H1-receptor in the left atrium triggers spontaneous diastolic depolarization, which may be involved in paroxysmal atrial tachycardia [26]. For example, the depolarization of purkinje-fibers induced by histamine has been reported to promote ventricular tachycardias [4]. In addition, rare cases of cardiac arrests and AF have been described in patients with clinically established hyperhistaminemia in mastocytosis and in anaphylaxis [27]. Because of its broad arrhythmogenic potential, and the lack of prospective data on the role of histamine in patients with AF, a pilot study was recently performed to evaluate plasma histamine concentrations

in patients with AF: there was a subpopulation of 10 patients with AF (21.2% of the enrolled subjects) that demonstrated clearly elevated levels of histamine [4]. In these patients, increased plasma histamine levels may be the result of ingestion of histamine containing food, allergic or pseudo-allergic reactions, infectious or immunologic disorders or other factors [28].

3.2. Role of Phenylethylamine, Tyramine and Trace Amines

Trace amines are defined as biologically active amines occurring in the body in trace amounts. They include β-phenylethylamine (β-PEA), tyramine, tryptamine and octopamine. They are structurally and functionally related to the catecholamines and there are a large number of synthetic analogues, such as the amphetamines. Tyramine, 2-phenylethylamine and putrescine are defined vasoactive amines as they result in increased blood pressure that can lead heart failure or brain hemorrhage [29].

Trace amines can also be found in the diet, deriving from plants, bacteria and fungi. PEA is a monoamine alkaloid with a stimulating effect, which is biosynthesized from the aminoacid L-phenylalanine by enzymatic decarboxylation. It is present in many organisms and foods, such as chocolate, especially after microbial fermentation [6]. Its pharmacological action is quite similar to amphetamine: PEA releases norepinephrine and dopamine [30] and after dietetic oral consumption it is quickly metabolized producing the amphetamine isomer N-methylphenethylamine. β-PEA was displayed to produce a stable increase in heart rate (about 55% over the baseline at 100 μM concentration).

Tryptamine, tyramine and octopamine displayed a positive chronotropic effect, approximately 30% over the baseline at a concentration of 100 μM [31]. These amines constitute sympathomimetic agents, which can act on the vascular system and determine vasoconstriction as well as increased blood pressure: these effects are mainly due to the release of noradrenaline from sympathetic neurons. In addition, they may exert a direct vascular effect through some novel amine-associated receptors (TAARs) identified in blood vessels, where trace amines can bind [32]. Tyramine is abundant in several fermented foods, such as goat's cheese (2000 mg/kg) [33,34] sausages (more than 200 mg/kg) [35] and probiotic foods, whose tyramine and β-PEA are generated by the high levels of lactic acid-producing bacteria, such as Lactococcus and Lactobacillus species [35]. Cocoa-based foods are important sources of tyramine and β-PEA, whose levels in cocoa range from 1.8 to 22 mg/kg [32]. Tryptamine is a trace amine and also occurs in diet, mainly in vegetables, such as tomatoes with concentration around 222 μg/g of dry weight [36]. Octopamine, which replaces noradrenaline in invertebrates as the main neurotransmitter in the sympathetic nervous system, also occurs in foods and foods supplements, such as bitter oranges (Citrus Aurantium), which additionally contains the alkaloid appetite-suppressor synephrine and a smaller amount of tyramine [37].

Cardiologists have recently recognized the great clinical and pharmacological relevance of trace amines, because of their sympathomimetic and, subsequently, cardiac effects [38]. These stimulating agents are often found in chocolate but also wine; in addition, they can be a constituent of medication with a potential arrhythmogenic risk [39]. For example, a case of AF related to chocolate abuse during anti-asthma therapy has recently been reported [40]. Even if a normal therapeutic dose of inhaled salbutamol, as well as a moderate consumption of chocolate, is not linked to the risk of arrhythmias, a chronic salbutamol treatment can increase the sympathetic responsiveness and slight β2-receptor tolerance; in addition, circulating catecholamines are responsible for the cardiac manifestations of theobromine and caffeine overdose toxicity.

A case of paroxysmal supraventricular tachycardia after dietary ingestion of a large amount of chocolate was reported [41]: a healthy adult woman showed palpitations and shortness of breath after ingesting a large amount of chocolate. ECG displayed a supraventricular tachycardia at 165 beats per minute, which was quickly restored to sinus rhythm after adenosine bolus injection. Electrophysiology studies displayed atrioventricular nodal reentry tachycardia, which was treated with radiofrequency ablation. This episode of tachycardia, precipitated by large amount of chocolate consumption in

a patient with an underlying substrate, happened because of cocoa methylxanthines (Figure 2), which are competitive antagonists of adenosine and may have arrhythmogenic potential [6] in particular conditions, such as during beta-agonist therapy or in presence of amine-rich foods, through a synergistic action.

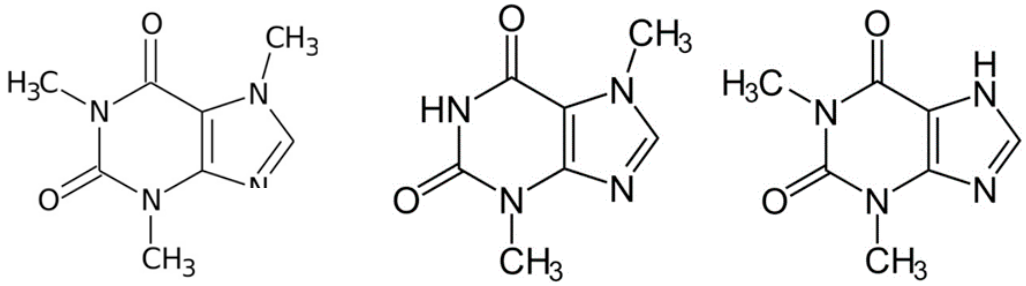

Figure 2. Molecular structure of metylxanthines in chocolate: caffeine (**a**), theobromine (**b**) and theophylline (**c**).

3.3. Role of Other BA

As well as histamine, other BA have been recognized as toxic amines with direct (tyramine) and indirect toxicity (putrescine, cadaverine, sperimine and spermidine). The indirect toxicity is correlated to enhance others Biogenic Amines activity, such as inhibiting metabolizing enzymes and promoting the malignant transformation of cells [22]. Their presence had previously been assessed even in ready-to-eat baby foods, being responsible for potential adverse reactions: restlessness and pseudo-allergic reactions, which can be due to sympathetic tone stimulation in infants and children [18]. BA analysis in baby foods has often evidenced high tyramine levels (1667 ng/g in fruit samples with banana) and very high polyamine levels (1263–53,416 ng/g) in samples containing green peas and beef [18] (Table 2).

Table 2. The main dietary biogenic amines (BA), the foods more at risk for their presence and their pharmacological effects.

BA	Foods More at Risk	Pharmacological Effects
Histamine [22]	Yeast extracts, cheeses, canned fish, red wines, spinaches, tomatoes	Headaches, sweating, burning nasal secretion, facial flushing, bright red rashes, dizziness, itching rashes, edema (eyelids), urticaria, difficulty in swallowing, diarrhea, respiratory distress, bronchospasm, increased cardiac output, tachycardia, extrasystoles, blood pressure disorders
Tyramine [22]	Chocolate, oranges, avocados, bananas, sauerkrauts, cheeses, raspberries, yeast extracts, fish, tomatoes, prunes, sausages	Headaches, migraine, neurological disorders, nausea, vomiting, respiratory disorders, hypertension
Phenylethylamine [42]	Chocolate, red wines, fermented foods	Releases noradrenaline, hypertension, migraine
Putrescine [22], Cadaverine, Spermine, Spermidine [43,44]	Foods in advanced stages of decomposition (meat and fish)	Increased cardiac output, tachycardia, hypotension, carcinogenic effects

3.4. Role of Alcohol and SULT1A Inhibitors

Alcohol ingestion (mainly red wine and sparkling wine) has often been reported as a trigger for AF [45], even if the pathophysiologic mechanism is not completely clear. Interestingly, especially red wine and sparkling wine have very high histamine concentrations [46], hence, histamine could be a trigger in alcohol-related AF. Thus, it appears worthwhile to further investigate whether systemic or local cardiac histamine may have supported or provoked AF. Another evidence of the cardiovascular impact of alcohol consumption concerns cytosolic sulfotransferases (SULTs) inhibition. SULTs enzymes

catalyze the sulfonation of both endobiotics and exobiotics: in particular, SULT1A enzymes protect humans from catecholamines. Natural substances in many foods were displayed to inhibit these enzymes in vitro [47], thus preventing normal catecholamine deactivation, leading to catecholamine increase, and subsequently blood pressure changes, migraine, palpitations and AF. SULT1A inhibition can cause the so-called "holiday heart" arrhythmias in susceptible patients, who probably have lower-activity SULT1A alleles. This alcohol consumption-related arrhythmia in healthy subjects may be due to catecholamines [48]. Several researchers have studied the in vitro inhibition of SULT1A enzymes by food constituents and additives. Nishimuta et al., [49] showed that orange juice, grapefruit juice and various teas significantly inhibit both SULT1A1 and SULT1A3. Chocolate, citrus, coffee, plants and many alcohols contain SULT1A inhibitors. Ice cream typically includes chocolate, fruit or plant-based flavorings such as vanillin or mint, and many sodas include natural flavorings from plants. It is commonly believed that a triggering ingredient in cheese is tyramine, however, several cheeses also include the natural food colouring annatto, which contains phenolics, such as hypolaetin and a caffeoyl acid derivative [50], and is most likely a SULT1A inhibitor. It is reasonable to hypothesize that an alcohol-based SULT1A inhibition, combined with a biogenic amines source (chocolate, cheese, ripened fruit or vegetable, stale fish or meat), can cause holiday heart in susceptible individuals. There is probably a genetic component to susceptibility to SULT1A inhibition, caused by lower-activity alleles of SULT1A1 and SULT1A3 [47].

4. Conclusions

An accurate assessment of cardiac arrhythmias always makes the investigation for underlying causes necessary. Recent research focused on the genetic basis of AF, leading to the identification of five novel loci [51], thus providing potential new molecular targets for future investigation and treatment. Not only genetics but also nutrition deserves further attention: food can directly or indirectly influence human health [52–54] and can be helpful in both the prevention and treatment of several diseases [54,55], in particular from a cardiovascular point of view [56–59]. Many clinical cases evidence a possible new relationship between some kinds of food and heart conduction (defining the very novel field of arrhythmogenic foods and of "nutri-arrhythmias") showing how chocolate intake abuse associated with chronic salbutamol [40] can trigger metylxanthines, as arrhythmogenic triggers an arrhythmia recognizing cocoa-rich foods abuse as the substrate for atrial fibrillation [6].

The possible involvement of histamine in cardiovascular disorders appears worthwhile to be investigated in view of histamine's and other BA-rich foods' pro-arrhythmogenic potential. Therefore, we suggest that anamnestic questionnaires in patients with new onset AF should include questions concerning not only allergic reactions during the last 24–48 h, in order to ask for histamine intolerance symptoms, but also an accurate food interview, in order to investigate any ingestion of histamine-rich foodstuff or other amines-rich food and alcohol consumption: their effects may result to be synergistic in alterating cardiac rhythm, thus configuring the very novel field of "nutri-arrhythmogenic foods" and of "nutri-arrhythmias".

Ethics approval and consent to participate: This study was approved by the Department of Medical Oral and Biotechnological Sciences, "G. d'Annunzio" University of Chieti-Pescara (approved date: 2 February 2018).

Consent for publication: The patient gave his consent to be described in anonymous way in this study: he provided his informed consent verbally for the publication of their information.

Author Contributions: M.A.G. designed the research and wrote the first draft; A.V. carried out the major revisions concerning the BA section; G.R. collected the data in literature; M.D.G. and A.D. revised the manuscript; N.D. had primary responsibility for the final content. All authors read and approved the final manuscript.

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Abbreviation

AF	atrial fibrillation
BA	biogenic amines
ECG	Electrocardiogram
H	Height
BW	body weight
BMI	body mass index
β-PEA	β-phenylethylamine
SULTs	cytosolic sulfotransferases

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