LETTER

Sudden cardiac death with morphologically normal heart: always do toxicology

BACKGROUND

Sudden cardiac death (SCD) is defined as natural unexpected death occurring within <1 hour in witnessed cases and within <24 hours of last being seen alive in unwitnessed cases. To assess the cause of death, many guidelines have been produced[1] and all toxicological investigation is essential. The term 'sudden adult death syndrome' (SADS) means an SCD where the heart is morphologically normal. It is well-known that many drugs increase the risk of ventricular arrhythmia.[2] This is the first study to assess the incidence of drug abuse and the characteristics of those with a normal heart who died suddenly.

METHODS

The analysis has been conducted reviewing all the 2021 cases received by the Cardiac Risk in the Young Centre for Cardiovascular Pathology at St George's University. Our centre refers hearts of SCD cases across all the UK, with an average response rate of 2 weeks. Circumstances of death and medical history were obtained from referral documents from the coroner, pathologist, general practitioner and a family questionnaire. For all the cases which showed a structurally normal heart, we suggest toxicological examination and, if the results are negative or not significant, we classify the death as SADS that needs genetic testing. Toxicology results were obtained retrospectively in all cases usually within 6 months of the autopsy and heart examination. Toxicological analyses aim to detect common substances of abuse and medications. In selected cases, other molecules (eg, new psychoactive substances) may also be investigated. After the analyses, the concentrations of various molecules found in biological fluids were assessed by an expert toxicologist. Finally, the toxicologist generates a report detailing the identified substances and their respective concentrations, along with comments on whether the substance or substances found could have played a causative role in the death.[3] The inclusion criterion of this study included all those cases where death was determined by the presence of one or more substances. Cases with negative or non-significant toxicology were excluded.

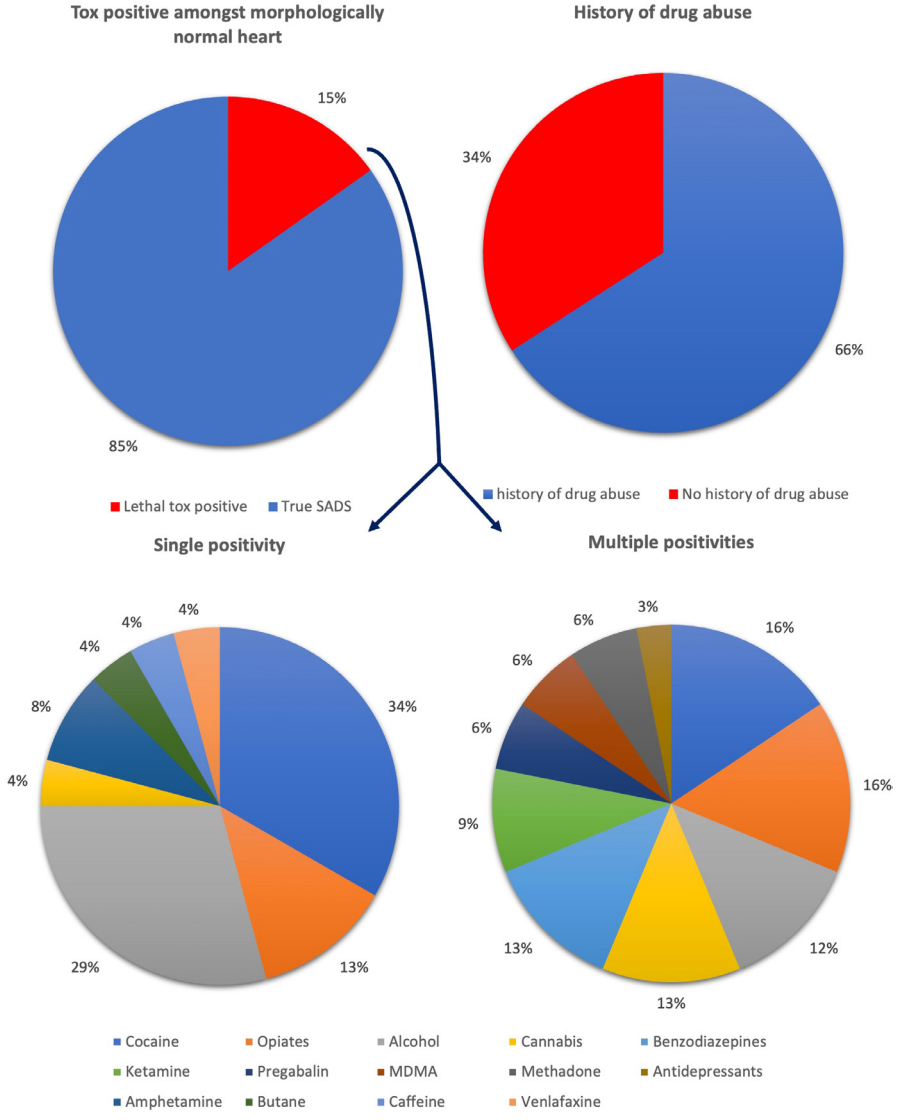

Figure 1 Summary of the toxicology positive findings. SADS, sudden adult death syndrome.

RESULTS

In 2021, our department received a total of 505 hearts, among which 270 were morphologically normal hearts. Toxicology results were obtained retrospectively in all cases usually within 6 months of the autopsy. Out of the 270 subjects who exhibited structurally normal hearts, 41 cases (15%) revealed lethal concentrations of one or more drugs based on the toxicological analyses. The mean age was 36±16 years old. 76% of the subjects were male. In 34% of cases, there was no history of drug abuse or suspicion raised from the circumstances of death. Overall, 56 substances were found in 36 individuals; for 5 subjects, the coroner's report mentioned only 'mixed drugs toxic levels'. Cocaine, alcohol and opiates were the most common substances found (32%, 27% and 20% of subjects were found positive, respectively). Single positivity was found in 24 cases, while multiple drugs were found in 41%. Among the single positivity, cocaine was the most common substance, followed by alcohol and opiates. In multiple drugs use, cocaine and opioids were the most common substances mixed. 21 subjects were older than 35 years, while 20 were younger. Single positivity (70%) and alcohol (29%) were more common in the older group, while multidrug abuse (52%) and cocaine use (38%) were more common in the younger group. A summary of the findings is provided in figure 1.

DISCUSSION

In 2021, the Office for National Statistics[4] registered 4618 drug-related deaths. The use or abuse of an unsuspected substance belongs in the differential diagnosis of patients who have died suddenly and

unexpectedly. Physical findings and the death scene may arouse suspicion that intoxication played a role in a patient's demise, but these suspicions may be absent. The experience from our department is that toxicology analysis must be performed in all cases of suspected SADS, no matter what the circumstantial evidence or the family information, as 34% of our positive cases reported no suspicious circumstances. If the toxicological analyses are not performed, those cases would be incorrectly classified as SADS, which means having unnecessary genetic screening and cardiological follow-up for family members. Sudden death due to drug abuse is the cause of death in 6% of SCDs[5] and 0.6–9% in sudden infant death syndrome.[6] These results demonstrate the need to consider toxicological screening in all postmortems. In Denmark, non-lethal toxicology positive cases were identified in 57% of sudden deaths.[7] This number is impressive as the inference of toxins at non-lethal levels may trigger a lethal arrhythmia due to genetic predisposition. We did not have details on non-lethal drugs found at autopsy in all our cases, which represents a limitation of our study. Our study highlights that toxicology analysis in the UK can take as long as 6 months, causing significant distress for families. Such a slow turnaround in providing toxicology results may cause a wrong labelling of the death as SADS until the results come out and the family member may enter the SADS pathway at Inherited Cardiac Clinics in the UK, with unnecessary cardiological and genetic screening. Early toxicology results will avoid this from happening. Our opinion is that similar results could be obtained if the toxicological analyses would be performed in cases of sudden cardiac arrest.

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