Cherry red spot: Evidence that its identification can speed up the diagnosis of GM2 gangliosdosis

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INTRODUCTION

A cherry-red spot is a finding in the macular of the eye which can be an indicator of several different lipid storage diseases. It was first described by Warren Tay in a patient with Tay–Sachs and its appearance is due to a relative transparency of the macula; storage disorders cause the accumulation of storage material within the cell layers of the retina[1]. The macula, which is relatively devoid of cellular layers, does not build up this material and a cherry red spot is revealed during ophthalmoscopic examination[2].

The GM2 gangliosidoses (also known as Tay-Sachs disease, Sandhoff disease and GM2-gangliosidosis, AB variant) are a group of these diseases and are caused by mutations in at least one of three recessive genes: HEXA, HEXB, and GM2A. The extent and type of GM2 gangliosidoses varies and diagnosis can be challenging due to the wide-ranging clinical presentation[3].

In a natural history study of the diseases, it was found that the diagnosis of GM2 Gangliosidosis can be challenging as the diseases can present in various ways and varying ages[3]. The infantile forms of will usually be picked up early as the child will fail to thrive, suffer from low muscle tone, have regular seizures and many other symptoms[4]. However, they are three of over eighty known lysosomal storage disorders where many have similar symptoms and this is what makes them notoriously difficult to diagnose and this can lead to a delay in a timely diagnosis[3]. Although a cherry red-spot is not a disease condition in itself, detecting it in a patient can lead to short-listing certain conditions, such as one of the GM2, followed by their speedy and correct diagnosis. A cherry red spot may be seen in certain individuals with a full-blown clinical picture of GM2 gangliosidoses. Its detection prior to clinical manifestation, e.g., in the Juvenile forms of Tay-Sachs and Sandhoff (it may be seen without clinical features) may aid in early diagnosis, planning for the future.

OBJECTIVES

The aim of the study was to determine whether identification of a cherry red spot can lead to an earlier diagnosis of GM2 gangliosidosis.

METHODS

Parents, carers and adults with GM2 gangliosidosis were recruited through the European Tay-Sachs & Sandhoff Charity Consortium (ETSCC) network. This consortium consists of the UK based The Cure and Action for Tay-Sachs (CATS) Foundation; the Spanish based Acción y Cura Para Tay-Sachs (ACTAYS); the German Hand in Hand gegen Tay-Sachs und Sandhoff; and the French based Vaincre les Maladies Lysosomales (VML).

Participants were recruited through social media and each of the charity's own communication channels. Using social media was important as it allowed the ETSCC to recruit participants from all over Europe, rather than just each charity's region. The survey consisted of thirteen questions and was made available via the online survey tool Survey Monkey. The questions were in English and all responses were anonymous.

RESULTS

Fifty people completed the survey from 10 European countries. Figure 1 shows that 68% of the participants suffered from Tay-Sachs (n – 34) and 32% suffered from Sandhoff disease (n – 16). Regarding the form of the diseases, figure 2 shows that 63% suffer from the Infantile variant of GM2, 32% the Juvenile form and 6% the Adult variant. Of the fifty participants in the study, 62% had a cherry red spot identified (n – 31) while 38% did not (n – 19). 84% of those who had a cherry red-spot had the Infantile, 16% had the Juvenile form and no participant with the Adult variant had a cherry red spot identified. Figure 3 shows the variant break down of the presence of a cherry red spot in each participant.

Figure 1. Diagnosis

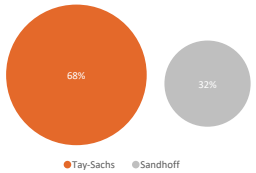


Figure 2. Variant diagnosis

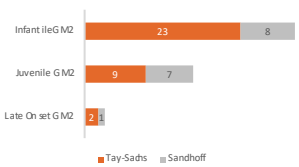


Figure 3. Percentage of GM2 variants with a cherry red spot identified

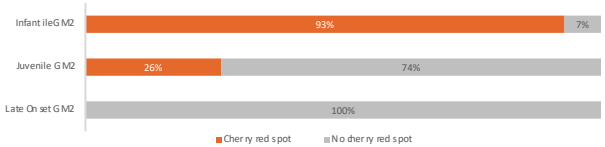


Figure 4. Time to diagnosis of GM2 after first contact with a healthcare professional

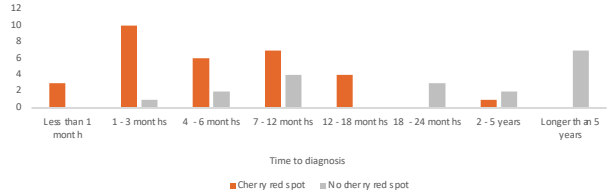
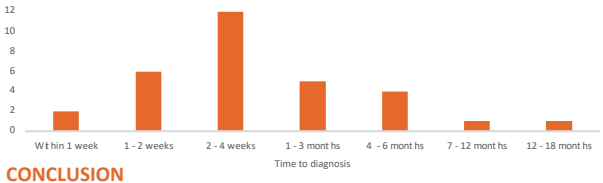


Figure 4 shows that for those people where a cherry red spot was identified the average time to diagnosis after presenting with the first symptom was 4-6 months while those where no cherry red the average time to diagnosis after presenting with the first symptom of was 18-24 month. Figure 5 shows that once a cherry red spot was identified the average time to diagnosis from identification to final diagnosis was 2-4 weeks.

Figure 5. Time to diagnosis of GM2 after a cherry red spot was identified



CONCLUSION

The benefits of a non-invasive eye test outweigh more laborious tests such as lumbar punctures, MRIs and biopsy's which are commonly performed during the diagnostic process for people who present with the common symptoms of GM2 gangliosidoses[3]. The study shows that investigating for a cherry-red spot is a useful tool as part of the diagnostic process for lipid storage disorders like GM2 gangliosidoses. Although a cherry red-spot does not present in everyone with GM2 gangliosidoses[5], it should still be one of the first tests considered by a neurologist if someone presents with the classic physical symptoms of GM2 gangliosidoses, such as failure to thrive, inability to roll over or sit up, and developmental delay[4]. However, the absence of a cherry-red spot in the neurologically impaired child or adult does not exclude these diagnoses but should form part of the overall diagnostic process[6]. Testing for a cherry red spot is not only vital in providing a definitive diagnosis to a family, but it also has a huge impact for any potential treatments in the future. Improving the speed of diagnosis is crucial to therapeutic efforts, because the window for intervention might be brief and later efforts might be futile it has been found that there is a point reached when functional deterioration and death cannot be prevented in an individual with GM2 gangliosidoses, but there is a small window of opportunity in which function and survival can be improved. Therefore, if a test for a cherry red-spot is performed immediately there is a higher chance of the disease being diagnosed quickly and the individual having the opportunity to have access to future treatments when they become available[6].

REFERENCES

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