Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) Media Backgrounder

Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS)

An Extremely Rare Autoinflammatory Disease

Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) is a rare autoinflammatory disease that can affect both children and adults\(^1,3\). This genetically inherited disease is characterized by long and intermittent attacks that can involve fever, abdominal pain, conjunctivitis, severe skin rash, swelling around the eyes and severe muscle and joint pain\(^1,3\). The condition is described as ‘systemic’ because its symptoms can affect the whole body.

TRAPS, formerly known as familial Hibernian fever, is one of three conditions that make up the hereditary periodic fever syndromes (HPFSs); along with hyperimmunoglobulinemia D and periodic fever syndrome (HIDS) and familial Mediterranean fever (FMF)\(^1\). The disease onset of TRAPS usually occurs later in life compared with the other HPFSs, with most patients developing the condition before the age of 20\(^1\). Males are more than 30% more likely to develop the disease than females but there is no gender specific difference in the symptoms of the disease\(^1,4\).

TRAPS is a rare disease, so few data exist on its incidence and prevalence. The prevalence of TRAPS in Germany in children under 16 years of age\(^5\) – and also in the UK population\(^6\) – has been estimated to be approximately one patient per one million individuals. There are currently no global prevalence or incidence rates for TRAPS\(^7\).

The role of inflammation in TRAPS

Mutations in \(TNFRSF1A\), the gene encoding Tumor Necrosis Factor (TNF) Receptor Type 1 (TNFR1), cause the signs and symptoms associated with TRAPS. Although the exact mechanism by which these mutations lead to TRAPS symptoms is unknown, several have been suggested\(^8,9\).

It has been suggested that, while mutated TNFR1 may still have the ability to bind strongly to TNF, the receptor cannot stay bound to the cell surface. This results in the build up of unbound TNFR1 within the cell which can result in the release of proinflammatory cytokines (immune signalling molecules)\(^8\).

Recent evidence suggests that, aside from TNF, other cytokines, such as interleukin-1 beta (IL-1 beta), may play an important role in the pathogenesis of TRAPS\(^10\). Patients with the condition have been shown to have an increased activation of NF-kappa B, a signalling molecule involved in the secretion of IL-1 beta and other proinflammatory cytokines\(^8,10\).

Unsuccessfully treated TRAPS can lead to severe complications

Amyloidosis is a serious complication of TRAPS and is estimated to occur in 25% of patients\(^11\). This long-term complication involves the production of a protein called serum amyloid A (SAA) during inflammation, and can lead to liver and/or kidney failure. In some instances, amyloidosis can be fatal\(^12\).
Diagnosis and treatment challenges
HPFSs, including TRAPS, often remain unrecognized and undiagnosed for many years and diagnosis can involve extensive investigation, including exploratory surgery. Misdiagnosis can also be a problem, as the symptoms of TRAPS can appear to mimic other conditions.

Currently, there are no approved treatments for TRAPS. Potential treatment options include nonsteroidal anti-inflammatory drugs and corticosteroids. While these have shown to relieve some of the symptoms associated with TRAPS, there can be problems with limited and intermittent efficacy. In addition, long-term corticosteroid use in children is associated with potentially serious adverse effects including growth suppression and delayed puberty. Research has also been undertaken into the use of anti-TNF compounds, although none have been approved for use in TRAPS to date.

With limitations in currently available treatment options and varying success of anti-TNF compounds, there remains a strong unmet need for therapies that can address the symptoms associated with TRAPS, including inflammation. The role of other cytokines in the pathogenesis of TRAPS is a promising area of research which could yield potential new treatments.

References

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