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Familial thrombophilic syndrome: MTHFR deficiency and risk of Covid-19 infection

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Background and aim of the work

The recent diffusion with Pandemia of the new Sars-Cov 2 infection [1,2] has introduced into clinical practice the need for the clinician to reconsider innumerable pathologies involving well known vascular risk factors. As a consequence, the treatment and the prophylaxis of the novel severe complications leading to increased mortality and disabling because suddenly urgent. Therefore, it has become necessary to revaluate pathologies incriminated for thrombotic risk even in 'unsuspected' young subjects due to the now assessed ability of Coronavirus infection to determine diffuse thrombosis. In fact in the protocols that came into use for the prophylaxis and therapy of Covid-19 infection is now practically validated the use of low molecular weight heparin. In this study the case of a young woman with methylenetetrahydrofolate reductase (MTHFR) [3] symptomatic deficiency diagnosed in the period of the Covid-19 emergency is reported. The same diagnostic questioning has also been extended to her family affected by this rare disease to prevent complications due to a possible Covid-19 infection.

Methods

We studied a young woman 24 years old suffering at least for ten years from migrant paresthesias initially sporadic and limited to parts of the upper limbs. The paresthesias initially appeared only in some positions of the arms, for example with the arms raised, leading the patient to think that they were due only to the position, while in the following years they intensified by extension, localization, and strength, also extending to the trunk and lower limbs regardless of the position taken. In the anamnestic collection, the patient reported that she was suffering from a family genetic pathology which she did not remember at that moment and which she did not relate in any way to the symptoms involved in the requested neurological examination. The author insisted to obtain the information about the nature of the genetic anomaly. The patient therefore ascertained the exact definition of her disease diagnosed several years before and reported that it was an 'MTHFR deficiency' which the author had already the suspicion. Her grandmother, mother, brother, and some first cousins were affected in her family by MTHFR deficiency. A genetic investigation with typing had been carried out in the affected and non-affected components of the family. Some of the relatives had been affected by hyperhomocysteinemia, while the patient had carried out on several occasions the blood dosage of homocysteine which had been at the upper limits of the norm. The genetic subtype that characterized her MTHFR mutation consisted of the A1298C and C677T subtypes which are among the most common in this type of mutation. The patient performed Brain Magnetic Resonance to check for signs of vascular damage and to exclude inflammatory processes, ultrasound of the arterial vessels to ascertain normal vascular flow, electromyography to check for signs of neurogenic damage.

Results

The instrumental investigations were normal. The patient was a non-smoker and had no other vascular risk factors. The clinical examination of the patient showed normality of the distrectual muscolar strength and anti-gravity test; Romberg's test was normal; osteo-tendon reflexes were diffusely, lively and symmetric with slight inversion of the radio-flexor reflex; she had not pain at the digital pressure of the spine; cranial nerves were normal.

Furthermore, there were no objective disturbances of sensitivity. The result obtained was the diagnosis of complications from MTHFR mutation probably related to an altered peripheral microcirculation and of the microcirculation of the vasa-nervorum in a patient previously considered asymptomatic.

Conclusion

Emerging epidemiological data related to the recent spread of Sars-Cov 2 infection have shown a clear prevalence in the older range age population. However, cases of young people who died or were seriously affected by the infection were described both in the chronicle of events and in the first studies carried out during the Pandemic. Any predisposing or 'protective' factors related to the age of the affected subjects are not yet known in the literature. Many hypotheses have been made forward regarding the greater susceptibility of elderly subjects to infection: among these the highest vascular risk especially following the observation that the lethality of Covid-19 infection is mostly linked to disseminated intravascular coagulation (CID) and thrombophilia while young ranges of ages are less affected. Many hypotheses are taken into account to explain lethality in the in the few affected young patients. Among these depressions of immune system or other diseases which give particular fragility. In some cases, however, no apparent plausible explanation has been called into question about the lethality of the infection. MTHFR deficiency hyperhomocysteinemia due to genetic

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mutation is a condition whose prevalence is unknown. The onset of any symptoms can occur at different stages of life from childhood to adulthood. It is transmitted as autosomal recessive gene. Diagnosis can be suspected by measuring homocysteine in the blood and may exhibit varying degrees of severity related to the mutation subtypes studied. Hyperhomocysteinemia can run asymptomatic or with underestimated symptoms leading to thrombophilic risk even at very young age. This condition must be kept in mind when diagnosing complications and mortality in the Sars-Cov 2 infection.

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