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# Erdheim-Chester disease is often complicated by neurological disorders

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## To the Editors

We were interested to read the article by Kaleta et al. about a 39-year-old man with Erdheim-Chester disease (ECD) who was diagnosed on the basis of typical clinical findings, a tibial plateau fracture, infiltration of CD68-positive histiocytes, and the presence of the V600E variant in BRAQ1 [1]. Clinically, he showed weight loss, gait disturbance, dysarthria, divergent strabismus, left hemiataxia, upper limb hypotonia and lower limb spasticity, pleural fibrosis, thickening of the interlobar septum, fibrosis of the kidneys, and fibrosis of the aorta [1]. Cerebral MRI showed thickening of the dura mater, pituitary stalk and skull bones, especially the frontal bones [1]. He was treated with vemurafenib, but there was no improvement [1]. The study is excellent, but some points should be discussed.

The first is that we disagree with the statement made in the title that the index case is the first case of ECD with neurological involvement in Poland [1]. In 2022, Chrostowska et al. reported a 40-year-old man with ECD diagnosed after clinical presentation and the presence of the BRAF V600E mutation. He had marked infiltration of the extraocular eye muscles to such an extent that the optic nerves were compressed and clinical visual impairment occurred [2]. Since skeletal musculature is the responsibility of a neurologist, and the optic nerve is not actually a cranial nerve but an appendage of the brain, it must be assumed that this Polish patient suffered from ECD with neurological involvement.

Our second point is that the spectrum of CNS manifestations of ECD is much broader than that described in the study [1]. CNS involvement in ECD can affect the hypothalamic-pituitary axis, the meninges, the cerebral arteries and the brain parenchyma [3]. CNS involvement in ECD can manifest not only in the form of cognitive impairment, seizures, headaches, ataxia, nystagmus, dysmetria, cranial nerve dysfunction, gait disturbances, sensory deficits and psychiatric problems, but also in the form of visual disturbances, diabetes insipidus, short stature, secondary hydrocephalus, pyramidal signs, peripheral neuropathy, cerebral atrophy, demyelination and/or neurodegenerative diseases of the CNS [4]. Abnormalities due to involvement of the anterior pituitary include secondary adrenal insufficiency, secondary hypothyroidism, growth hormone deficiency, and hypogonadotropic hypogonadism [5]. Impairment of the posterior pituitary gland can lead to hyperprolactinemia or hypoprolactinemia [5]. The CNS may even be the only manifestation of ECD if no organs other than the brain are affected [6]. In a single ECD patient, a double subclavian steal syndrome has been reported as a vascular and neurological manifestation of the disease [7].

The final point is that ECD can also be complicated by secondary cerebral disease due to primary involvement of the heart, e.g. ischaemic stroke or cerebral haemorrhage. Hypoaldosteronism can be complicated by seizures.

In summary, the excellent study has some limitations that should be addressed before final conclusions can be drawn. Clarification of these weaknesses would strengthen those conclusions and improve the study. Since neurological involvement can occur in almost half of patients with ECD, and the average delay in ECD diagnosis is four years, neurologists should consider ECD in patients with inflammatory,

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infectious, or neoplastic-appearing white matter changes due to infiltration of CD68-positive histiocytes. It must also be considered that cerebral disease may be the first, or even the only, manifestation of ECD.

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