Calvarial thickening due to anticonvulsants other than phenytoin

Z Siddiqui[1], K Singh[2]

Image in medicine

Consent: Written consent obtained from patient

Declaration of interests: No conflict of interests declared

Correspondence to:
K Singh
Heart of England NHS Foundation Trust
Birmingham

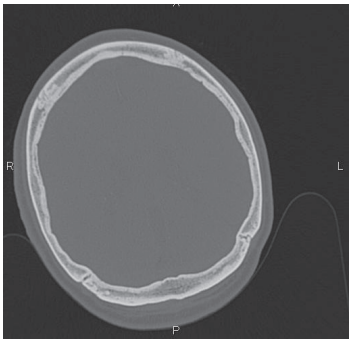
Email:
kanwaljit.singh@nhs.net

A 53-year-old Caucasian man with known frontal lobe epilepsy presented with a tonic–clonic seizure. The patient had been treated previously with multiple anti-epileptic drugs (sodium valproate, carbamazepine, clobazam). During his admission he suffered a further three seizures overnight and underwent a CT head scan to rule out a new symptomatic cause. The CT head (Figure 1) did not show any acute intracranial pathology; however, it demonstrated bilateral calvarial thickening. The patient underwent an electroencephalogram which did not show any evidence of encephalitis. His blood tests, including parathyroid hormone, were satisfactory.

The drug most commonly associated with calvarial thickening is phenytoin.[1,2] The pathological mechanism of action has been suggested to be upregulation of transforming growth factor-beta1 and bone morphogenic proteins, which in turn increase osteoblast proliferation.[3]

Our patient confirmed that he had never been given phenytoin. However, he demonstrated the same radiological features typical for chronic phenytoin use. Other possible causes of calvarial thickening, e.g. osteopetrosis, acromegaly, and hyperparathyroidism, were not present in our patient. Calvarial thickening is generally a benign condition, apart from cosmetic issues, and does not seem to have much clinical significance. Some studies have suggested it can influence the estimation of brain atrophy especially in older women.[4] The average skull thickness in males is up to 6.5 mm and females up to 7 mm. One study suggested that the difference between male and female skulls was more towards the rear of the parietal bones. The mean thickness of the skull across all locations was 6.32 mm. It ranged from 5.3 mm to 7.5 mm.[5]

Figure 1 CT head showing bilateral calvarial thickening



The radiological findings on the CT head of our patient leads us to consider whether there are other anti-epileptic drugs that may result in long term phenytoin-like changes in the form of calvarial thickening. Further research into this area and reporting of similar cases might help to establish such a link.

References

1 Kattan KR. Calvarial thickening after Dilantin medication. *Am J Roentgenol Radium Ther Nucl Med* 1970; 110: 102–5.
2 Lefebvre E, Haining R, Labbe R. Coarse facies, calvarial thickening and hyperphosphatasia after anticonvulsants. *N Engl J Med* 1972; 287: 721–2.
3 Chow K, Szeto C. Cerebral atrophy and skull thickening due to chronic phenytoin therapy. *CMAJ* 2007; 176: 321–3.
4 Royle NA, Hernandez MC, Maniega SM et al. Influence of thickening of the inner skull table on intracranial volume measurement in older people. *Magn Reson Imaging* 2013; 31: 918–22.
5 Moreira-Gonzalez A, Papay FE, Zins JE. Calvarial thickness and its relation to cranial bone harvest. *Plast Reconstr Surg* 2006; 117: 1964–71.

[1]Foundation Programme, Trainee, Health Education West Midlands; [2]Consultant Geriatrician, Heart of England NHS Foundation Trust, Birmingham, UK