



ADVERSE DRUG REACTIONS, INCLUDING SJS, TEN

EMPACT SYNDROME ASSOCIATED WITH PHENOBARBITAL INSTEAD OF PHENYTOIN: A NEW CLINICAL ENTITY.

L. Panariello⁽¹⁾ - M.c. Annunziata⁽¹⁾ - M. Vastarella⁽¹⁾ - G. Fabbrocini⁽¹⁾

University Of Naples Federico II, Department Of Clinical Medicine And Surgery - Section Of Dermatology, Naples, Italy⁽¹⁾

BACKGROUND: EMPACT syndrome is a rare clinical entity characterized by “Erythema Multiforme associated with Phenytoin and Cranial radiation Therapy”. It is characterized by erythema multiforme-like lesions which develop in patients affected by brain metastasis, who are treated with cranial radiotherapy and phenytoin to prevent seizures. The eruption typically starts at the cranial radiation site and subsequently spreads over a few days to involve extensive areas of the body.

To date, over 30 cases of EMPACT syndrome have been described in the literature, all of them developed in patients under phenytoin treatment.

OBSERVATION: We report 3 cases of EMPACT syndrome that occurred in patients on phenobarbital therapy instead of phenytoin.

Each patient, after the exclusion of an infectious etiology, started a therapy with systemic steroids, obtaining a complete resolution of manifestations after 30-40 days.

The pathogenesis of EMPACT syndrome is still unclear. Radiation can alter anticonvulsant drug metabolism. In fact phenytoin induces microsomal cytochrome 450(CYP)3A, producing oxidative intermediates that are subsequently detoxified by epoxide hydrolase. The association of phenytoin and radiation therapy can lead to a deficiency of this enzyme, so that oxidative intermediates can not be metabolized. These intermediates are directly toxic to cells and/or they can bind to cell macromolecules, behaving like haptens. These mechanisms can stimulate a secondary immune response. Since barbiturate detoxification too is mediated by epoxide hydrolases, this might also explain how phenobarbital can be responsible for EMPACT syndrome.

KEY MESSAGE: On the basis of our reports, it is important to alert physicians about the risk to develop EMPACT syndrome in patients treated with antiepileptic drugs, in particular phenytoin and phenobarbital, who start radiotherapy. An alternative therapy for seizure prevention should be considered, such as gabapentin or levetiracetam, neither of which is metabolized by this detoxification pathway.

