Status dystonicus present in an acute osteosarcoma cell culture on collagen.

METHOD

Gelatinase expression, assessed using zymography of supernatant, demonstrated increased proMMP-2 activation by cells cultured on collagen, particularly by U2OS cells. Cell lysates were probed for MT1-MMP using western blotting. ELISA of the cultured supernatant was used to measure TIMP-2 expression. Less active MT1-MMP was detected in the lysates of the U2OS cells which coincided with a decreased amount of TIMP-2 detected in the supernatant.

RESULTS

Resolution of the movement disorder and fever and normalization of CK followed. He re-presented a month later with similar symptomatology; however, early treatment with hydration, clonidine and chloral hydrate appeared to halt progression to status dystonicus. He went home on low-dose clonidine and remains well.

CONCLUSION

Status dystonicus is a rare condition with a high morbidity and mortality. A rising CK, severe dystonic movements and metabolic derangements suggest the diagnosis. Maintaining a high index of suspicion can identify such cases early and halt further progression. CK is simple test to monitor response to treatment.

OSTEOSARCOMA CELL CULTURE ON COLLAGEN SURFACES AND IN HYPOXIA ALTERS MMP EXPRESSION

Osteosarcoma is the most common primary malignant bone tumour in children. The survival rate has not improved much over the last 25 years, and therefore there is a lot to learn about the pathogenesis of this cancer. The interactions of tumour cells with their environment and hypoxia have been identified as key drivers of tumour growth and metastasis. Matrix-metalloproteinases (MMPs) are involved in this process. MMPs are zinc-pectidases that are able to degrade the extra-cellular matrix and are over-expressed in many tumours. Membrane-type (MT1)-MMP and MMP-2 expression is positively associated with tumour progression in a range of tumours, but their role is not well characterised in osteosarcoma.

Two osteosarcoma cell lines were cultured on culture plastic or collagen surfaces in either normoxia or hypoxia. Proliferation was assessed using the SRB assay which showed osteosarcoma cells proliferate slightly slower in hypoxia. Immunofluorescence microscopy was employed to visualise MT1-MMP – this revealed MT1-MMP packaging and localisation was altered in hypoxia and there was formation of invadopodia on collagen. Gelatinase expression, assessed using zymography of supernatants, demonstrated increased proMMP-2 activation by cells cultured on collagen, particularly by U2OS cells. Cell lysates were probed for MT1-MMP using western blotting. ELISA of the culture supernatant was used to measure TIMP-2 expression. Less active MT1-MMP was detected in the lysates of the U2OS cells which coincided with a decreased amount of TIMP-2 detected in the supernatant.

This study contributes to our understanding of the activation of MMPs and the possible role of MT1-MMP in this regard.

FIBRODYSPLASIA OSSIFICANS PROGRESSIVA (FOP) AN UNFAMILIAR DISEASE THAT IS NOW IMPORTANT TO DIAGNOSE

FOP is a rare but disabling condition characterised by congenital malformation of the great toes and progressive heterotopic endochondral ossification (HEO). FOP is the most catastrophic disorder of HEO in humans.

Flare-ups are episodic; immobility is cumulative. The discovery of the ACVR1 gene as the cause of FOP has allowed identification of possible therapeutic targets. Palvocetin, a retinoic acid receptor gamma agonist, is currently in Phase 2 clinical trials to reduce HEO during acute flares.