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STUDY THE PATHOLOGICAL EFFECT OF VINBLASTINE ON BON AND BRAIN IN GUINEA PIGS

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ABSTRACT
The present study was designed in order to identify the pathological effects of Vinblastine on brain and bon in guinea pigs. Forty mixed animals were used, injected with Vinblastine in dose of (1mg/10gm B.W) for (2, 4, 6) weeks, in separated three groups, the results showed that there were marked vacuolation in neurons with congestion in brain tissue with haemohrage and inflammatory reaction in bone tissue after 2 weeks of injection; with haemohrage and perinuronal edema of brain tissue and incomplete calcification of bone tissue after 4 weeks of injection ; with marked gliosis of brain tissue and low intensity of bon and clear haemohrage and inflammation with necrosis and abnormal calcification after 6 weeks of injection. Conclusion vinblastine caused clearly damage to brain and bon within two weeks.

KEY WORD: Vinblastine, Guinea Pigs, bon, brain.

INTRODUCTION

Vinblastine was extracted from the leaves of plant *Catharanthus roseus* and used for treatment different viral and non-viral diseases; tumors or chronic diseases[1]. But clinically uses were careful due to its' sensory motors' neuronalpathies[2]. Diab Kathar *et al*.[3] said that vinca alkaloids induce caused chromosomal abnormalities in bone marrow cells. And neurons' tissue damage [4]. Within few weeks there is marked singes of cell death[5] and myelosupperssion due to its effects on bon and related tissues[6,7], such as peripheral nerves, sciatic nerve[8]. Pathological lesions appeared in brain, spinal cord, dorsal root ganglia, neuromuscular junction and skeletal muscle in guinea pigs, at acute and chronic period [9] and in lab animals increase in the synapse sensory nerve action [10,11]. In Cat, author [12,13] described focal axonal swelling (giant axon formations) and edema due to maligned accumulation of neurofilmants and secondary demyelization. Cerebellum development has been studied by author[14] in pregnant mice after exposure to Vinblastine in day of 10 and 15 of pregnancy duration newborns selected to histopathological examination, white matter of cerebellum showed increasing interstitial space and decreasing in compacting neuroglia cells accompany with deficiency in myelin's neurons fibers, occurring of apoptosis were seen in epithelial cells of choroid network and white matter neuroglia cells. In rats', spinal injury with diabetic neuropathy and white matter ischemic injury induced by vinblastine[15]. Also there were skeletal disorder represented by osteoporosis and osteomalacia with born loss, osteoporosis responsible for increased propensity to fracture, the mechanism of this effects due to inhibits the proliferation and differentiation of osteoblasts and selectivity reduces in normal stapeses of bone formation through alteration in osteoblasts' receptor [16-19]. Authors[20, 21] and explained effects of vinblastine in canine bone marrow and male mice and revealed that the most striking cytological changes were observed on bone marrow precursors cells at metaphase and caused in signs as increased numbers of mitotic figures abnormal nuclear configurations and fragmented nuclei.

MATERIALS & METHOD

Forty mixed guinea pigs were kept in animal house of Baghdad Vet. Medicine College and fed on pellet for lab. Animal, and provide with tap water in special bottles , and injected with Vincristine by I/P(0.1mg/10gm b.w) for three separated period of time (2,4,6) weeks, at three separated subgroups each subgroup contain 10 animals and remaining 10 animals consider as control injected with distilled water[22] after scarified animals at each end of each interval, tissue samples of brain and bone were prepared from each animal and tissues' processing were done [23]**.** Then staining methods were performed [24]**.**

RESULTS & DISCUSSION

1-Results of 1st group

A-Brains' tissue changes: pathological findings in brains' samples in the 1st subgroup showed, that there were marked vacuolation of neurons with congestion (Fig.1)10X.

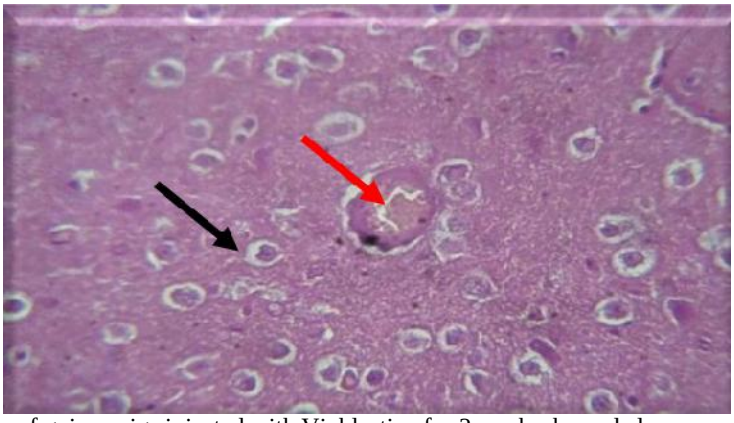
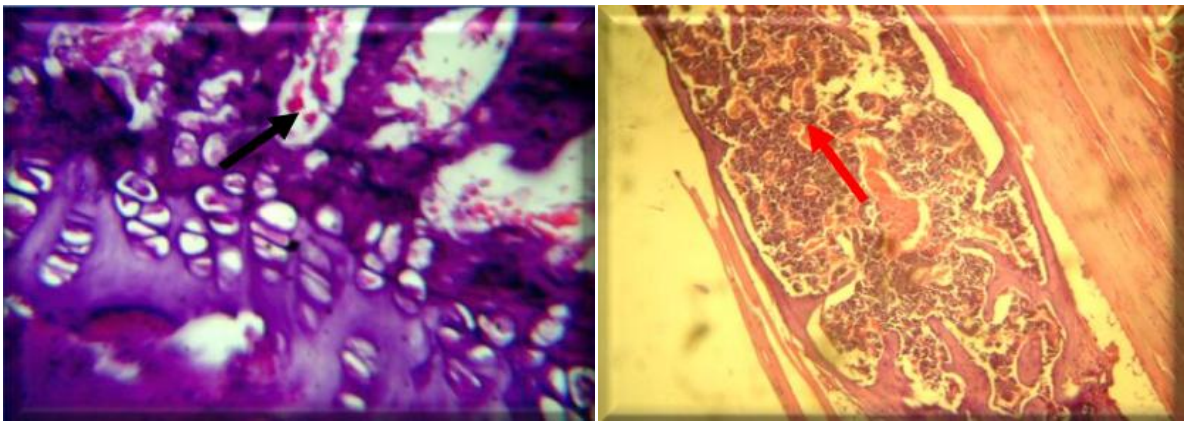


FIGURE 1: Brain tissue of guinea pigs injected with Vinblastine for 2 week, showed clear vacuolation in neuron (black arrow) with congestion (red arrow).

B-Bones' tissue changes: pathological findings in bones' samples in the 1st subgroup showed, that there were clear haemohrage and inflammatory reaction (Fig.2: A.400X, B.100X).



A **B**

FIGURE 2: Bon tissue of mouse injected with Vinblastine for 2 week, showed haemohrage (black arrow) and inflammatory reaction (red arrow).

These observations in brains' and bones' tissues of guinea pigs treated for two week, occurred as a result of the non-cell specific toxic effects of Vinblastine within few hours to few weeks, which associated with early signs of inflammatory reaction as infiltration for different type of cells included R.B.C_s.(red blood cells),W.B.C_s (white blood cells).

2nd group

A-Brains' tissue changes

Pathological findings in brains' samples in the 2nd subgroup showed, that there were haemohrage and perinuronal edema with destructive changes (Fig. 3).

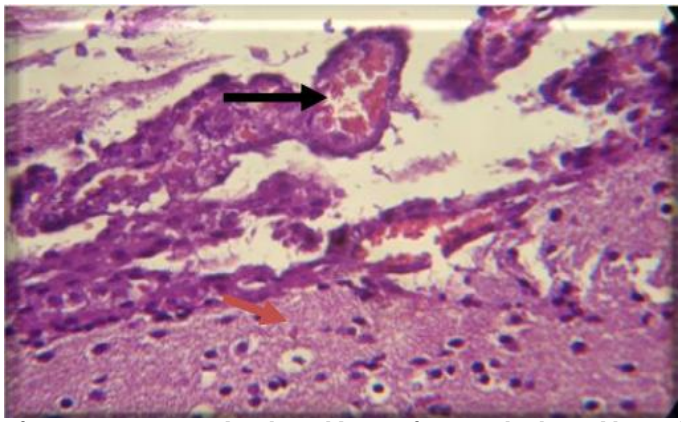
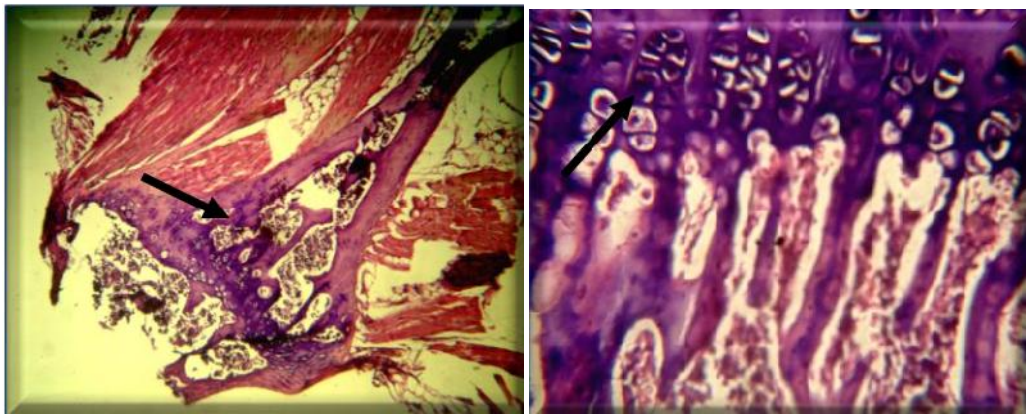


FIGURE.3: Brain tissue of guinea pigs injected with Vinblastine for 4 week, showed haemohrage (black arrow) with perinuronal edema (red arrow) 100X.

B-Bones' tissue changes

Pathological findings in bones' samples in the 2nd subgroup showed, that there were incomplete calcification **(**Fig. 4: C: 100 X, D: 400X).



C **D**

FIGURE 4: Bon tissue of guinea pigs injected with Vinblastine for 4 week, showed incomplete calcification (arrow).

These pathological changes in brain and bone tissues of guinea pigs treated for four week refer to continuously and directly effects of Vinblastine on cell of brain and bone.

3rd group

A-Brains' tissue changes

Pathological findings in brains' samples in the 3rd subgroup showed, that there were marked gliosis of neurons (Fig. 5).

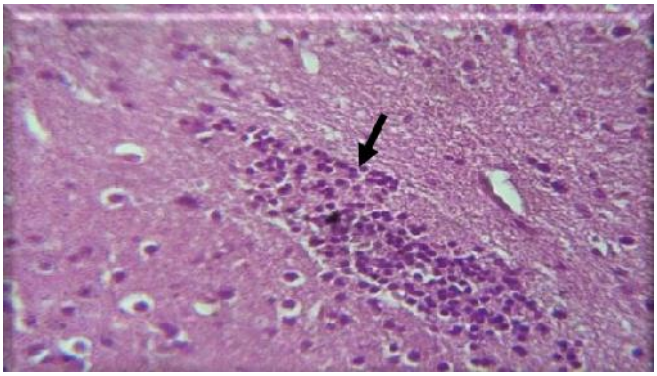


FIGURE 5: Brain tissue of guinea pigs injected with Vinblastine for six week, showed evidence of gliosis (arrow) 100X.

B-Bones' tissue changes

Pathological findings in bones' samples in the 3rd subgroup showed, that there were low intensity of bone cells (osteoblasts) with clear haemohrage and inflammatory reaction with incomplete calcifications (Fig.6, E: 400X, F: 100X).

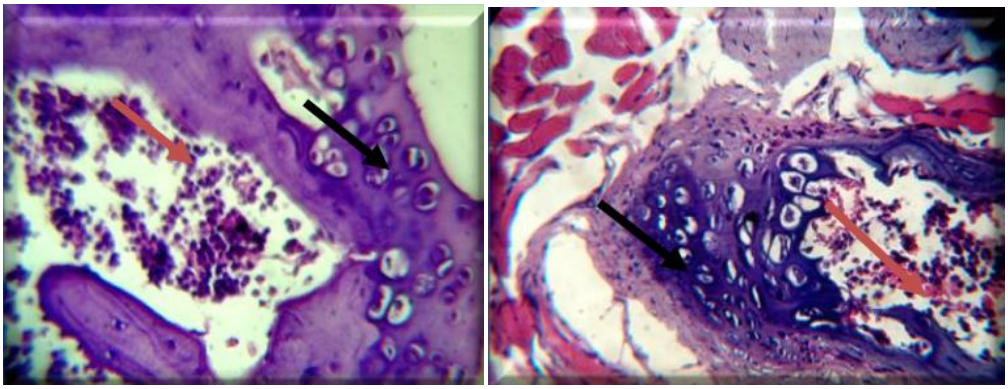


FIGURE 6: Bon tissue of guinea pigs injected with Vinblastine for six week, showed low intensity (black arrow), haemohrage (red arrow) in each figures (A, B).

Investigations on brain tissue's showed that there were evident of neuronal vacuolation due to hydropic degeneration with congestion due to neuronal injury and gliosis due to lose normal size and volume after loss of fluid. On bone tissue's pathological lesions represented by haemohrage and inflammatory reaction and lose of normal calcification and bon intensity due to incomplete osteoblasts maturation, and this finding agree with authors [2,4,18,20,21], opinions of neuronal tissues and brain changes and agree with authors [3,9,11,14,25], opinions about bone tissues changes due to vinblastine effects.

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