

Aplastic Anemia In Two Siblings Due To Use Of Organochlorine Pesticide Lindane

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Received Date: 27 February 2024

Accepted Date: 12 March 2024

Published Date: 20 March 2024

Citation:

Yurdanur Kilinc. Aplastic Anemia In Two Siblings Due To Use Of Organochlorine Pesticide Lindane. Journal of Clinical Cases 2024.

1. Introduction

Aplastic anemia (AA) is a hematopoietic disorder with high risk of death and characterized by pancytopenia and hypocellularity of bone marrow. The suspected etiological factors are the losses and/or functional disorders of the stem cells, ultrastructural defects of bone marrow elements, abnormalities of regulatory growth factors in blood and autoimmune inhibition of hematopoiesis [1]. Although the incidence of aplastic anemia is [3-5] per million in the general population, [2-4] per million in childhood under 15 years and is more frequent in the eastern countries compared with western countries; the Asiatic populations are [2-3] fold more than the other populations [3-7]. Also, illiterate people have higher risk for acquired aplastic anemia. Many drugs have been shown as causative agents in AA [8,9]. These drugs are composed of benzene rings (e.g. chloramphenicol). One of the most important associations in the aetiology

of AA is pesticide consumption. [10] The affinity of the organochlorine pesticides to lipid tissue is very high and they accumulate there. The objective proof for important concentrations of the product of of tissue pesticides may confirm the exposure to these agents before [9]. In this paper, the presence of organochlorine pesticides Lindane (γ-hexachloro cyclohexane, HCH) and DDT (dichloro-diphenyl trichloroethane) in fat tissue have been shown by gas-liquid chromatography (GLC) method and acetylcholinesterase (ACE) values in serum by Ellman method. In two siblings after exposure to Lindane (G-hexachlorocyclohexane). T cells accept the antigenic stimuli and transfer to B cells. First of all, T-cell mediated immunity may be convenient in case of many mature T cells AND must be settled in secondary lymphoid organs. As a result, rich TC Accumulation in this cell population, all foreign antigenic stimuli may be recognized. TCR (T cell receptors) complex is multimolecular and by way of the capability of binding city, TC Produces The activation signals for the B cells .

2. Case1

O.S.7 year-old girl was admitted to the Pediatric Haematology follow-up clinics with the complaints of epistaxis, bruising in arms without pain and weakness. Parents confirmed that she was healthy till one year. First, she had had bruising one year before and epistaxis began last ten months, she was improved with medical care, but epistaxis was repeated two months before admission to the hospital. At that time, she was referred to University Hospital with the complaints of fever, paleness and weakness by a pediatrician. In family history, fathers have applied the aerosol Lindane on the body surface of his children against mosquito bites during summer time in the last two years. On admission, she appeared pale, had had petechiae different sites of her body and ecchymotic areas were seen on her left forearm and she had had an infected lesion at the left upper side of her lip. Her pharynx and tonsillar were infected. Other system findings and neurological examinations were in normal limits. Informed Consent Was Received From The family for both siblings for publication. She had Pancytopenia. As Seen On Table 1. Hb Was 9.0g/dl; PCV 27%, WBC count 3000/mm³; absolute neutrophil count was 900/mm³, platelet count 90.000/mm³.

Days	0	1	2	3	4	5	6	7	14
Hct%	36	35	33	31	34	35	35	33	35
Retics%	1.6			1				1	
WBCs/m	4400	1800	2400	3600	4600	4800	3600	2000	5000
m3									
Platelets/ mm3	80.000 0	70.00 0	90.000 0	40.000	110.000	120.00 0		130.00 0	

Table 1: Hematological datas of Case O.C.

On bone marrow aspiration biopsy, significant decrease in numbers of all hematopoietic precursor cells were seen. Ivy bleeding time was longer than 13.3 minutes, whole blood clotting time was 7 minutes. The other coagulation testswere in normal ranges. The renal and liver function tests were normal. The storage HCH (γ-hexachlorocy clohexane) and PPI-DDT concentrations in fat tissuesamples were investigated. Serum acetylcho line sterase level measured by Ellmanmethod was 0.48 IU/mL (normal 1.5-3.5 IU/mL). The amount of fat in subcutaneous tissue was 33.96%; the amount of γ-HCG was 1.37mg/kg/ fat tissue; PPI-DDT was 3.38 mg/ kgfat tissue (Table 3). Thepatient was supposed to have aplastic anemia due to exposure to toxic agentLindane. Prednisone 3mg/kg/day p.o. and Oxymetholone 2mg/kg/ day was begun forsupportive therapy. The patient was in follow-up for daily CBCs (Table 1, Figure 1). In two weeks, haematological parameters were close to normal values. The dose of Prednisolone Was tapered transiently and stopped in three weeks, oxymetholone was given alone. In two months, bone marrow aspiration biopsishowed significant increase close to normal values incellularity.

Figure 1

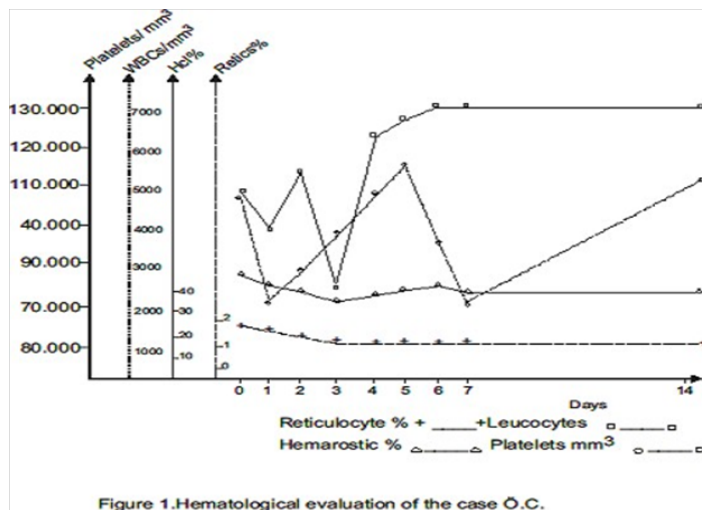


Figure 1. Hematological evaluation of the case O.C.

3. Case2.

H.C, a 5 year-old boy was the brother of the first case. The parents informed thathe had bruised spontaneously or after a trauma in different sites of his bodysince two and a half years and recently, these lesions were seen morefrequently. On admission, system findings- except ecchymo season

hisar sandlegswere found normal. Neurological Examination Were found in normallimits. The patient have aplastic anemia due to exposure to toxic agent Lindane. Prednisone 3 mg/kg/ day p.o. and Oxymetholone 2mg/kg/ day was begun for supportive therapy. The patient was in follow-up for daily CBCs (Table 2, Figure 2). In two weeks, haematological parameters were close to normal values. The dose of Prednisolone decreased and stopped pedi three weeks, The oxymetholone given alone. Into Months, bone marrow aspiration biopsy showed significant increase çölse tonormal values in cellularity. His hematological evaluation was as follows: Hb 11.6g/dl; PCV 36%, WBCs 1800/mm³; absolute neutrophil count 450/mm³; platelet count 40.000/mm³; bleedingtime 10 mins, whole blood clotting time 8 mins. The other coagulation testswere found normal. Serum sample and biopsy sample taken from subcutaneous fat tissue were being investigated for organochlorine HCH. Acetyl Level was 2.79 IU/mL (N 1.5-3.5IU/mL) in the serum sample . The fat tissue amount was %23.88; β- HCH was1.84mg/kg tissue; PPI-DD Amount was8.23 mg/kg fat tissue (Table3). Bone marrowaspiration biopsy specimens had shown significant hypocellularity. He wasassumed to have aplastic anemia due to the toxic agent Lindane. As was in thefirst case, supportive therapy was begun with Prednisolone and Oxymetholone andhaematological profile was followed with daily CBCs (Table 2, Figure 2). After 2weeks of treatment, significant improvement was observed. In 3 months, the bonemarrow aspiration specimen was at normal limits in cellularity.

Figure 2

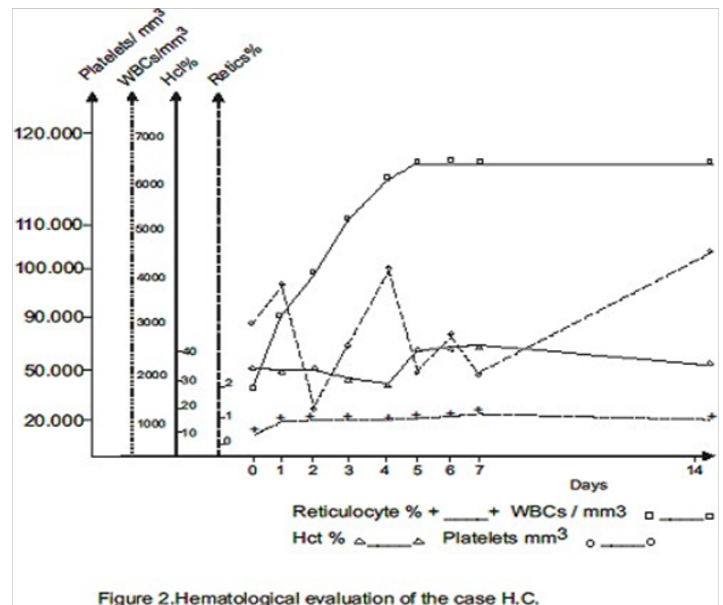


Figure 2. Hematological evaluation of the case H.C.

Days	0	1	2	3	4	5	6	7	14
Hct%	27	25	26	23	23	35	39	38	35
Ret%	0.1			1.2				1.2	
WBCs/mm ³	3000	3600	1000	2600	4200	1600	2600	2000	4000
Platelets/mm ³	20,000	50,000	90,000	100,000	110,000			120,000	

Table 2: Hematological datas of Case H.C.

4. Discussion

Lindane as is found in the structure of DDT; is accumulated in human fat tissue after exposure [11]. The processed wooden stuff is free of insects for years; this shows the biological activity of pesticides is continuous. The evaporating pressure is low for lindane and it can be separated easily from heated containers: lindane may be absorbed transcutaneously from lungs or gastrointestinal tracts. Lindane may be taken as gamma isomer and following ingestion it is stored as gamma isomer in fat tissue: it is partially metabolised to pentachlorophenol and to the other phenols in liver: in acute lindane intoxication; it is caused to central nervous system impulses and convulsions especially in children. In case of chronic exposure to lindane, major toxic effects may be seen in the liver as disorders of microsomal enzyme system damage of the liver and tumour formation in liver in experimental animal studies. In human beings, some aplastic anemia cases are reported from the epidemiological studies for a long period of exposure to Lindane. The first cases are reported from the USA and after that time it is forbidden to use in household usage [15]. In 1979, 30 cases of aplastic anemia were reported due to only lindane exposure and 10 cases of aplastic anemia due to other compounds together with lindane [15], and consumption of lindane was forbidden. Aplastic anemia was more frequent in rural residents compared with urban areas. In addition to host genetic predisposition, several other hematotoxic risk factors may contribute to an environmental etiology of aplastic anemia [16]. Occupational exposure to pesticides among farmers associated with all kinds of hematopoietic cancers [17-18].

Table 3: Pesticide values of two siblings

	Fat tissue %	γ-HCH (mg/kg fat)	PPI-DDT (mg/Kg fat)	Serum acetyl cholinesterase (IU/ml)
Ö.C.	23.88	1.84	8.23	2.79
H.C.	33.96	1.37	3.38	0.48

The effect of Lindane on bone marrow is mostly idiosyncratic marrow depression; it shows this effect by the change of T helper/T suppressor ratio in favour of T suppressor cells [18-19-20]. In our report of two siblings, aplastic anemia is seen as a result of long term use of Lindane. It's interesting that; in addition to Lindane, there was quite a high amount of DDT in excessive concentrations in fat tissue and serum acetylcholinesterase levels were low in both siblings. Linda Neis consumed in both in home consumption or in gardens in agricultural areas in our country. The presence of DDT in high concentrations in our cases shows that this agent is used unconsciously in rural areas both in household stuff and in farms as an insecticide in our country. In these two siblings mentioned above, DDT concentrations were very high and their parents were not aware of toxicity of Lindane. It is very important

to educate people about the set of oxigens and their effects on human health and prevention of exposure to these substances. The consumption of pesticides must be regulated in accordance with a law and it must be restricted for some limited areas where the usage is necessary under the control of the government. If it is possible, the consumption of pesticides must be forbidden in populated areas.

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