PharmacologyOnLine April 30, 2014

Case Report • 2014 • vol.1 • 1-6

AN AVOIDABLE FEMALE DEATH: CASE REPORT OF INAPPROPRIATE MEDICATION

Komal Farooq

Department of Pharmacy, University of Sargodha, Sargodha, Pakistan

Komalfarooq22@gmail.com

Abstract

Interstitial Lung Disease (ILD) is a diverse collection of ≥ 200 lung disorders. it affect the compartments of the lung; alveolar tissue, interstitium , trachea, bronchi, and bronchioles. Most interstitial lung disease is characterized by physical symptoms like radiographic abnormalities, altered pulmonary function and distinctive inflammation fibrosis. Because of its epidemiological risks we aimed the case study of 38years female, 81kg, having dyspnea. She was presented in local clinical setting. The clinical examinations drive the physicians toward ILD. Therefore, on behalf of her current investigation/ findings the pulmonologist prescribe Endoxan(Cyclophosphamide) 50mg 2 tablets OD (one a day), Nexum(esomeprazole)40mg OD, Deltacortril enteric coated (Methyl Prednisolone) 4 tablets in morning, Xynosine nasal spray, Citanew 10mg OD. The therapy was continued for one year. She was then diagnosed with benign breast cancer. Consultant oncologists suggested and then did mastectomy of right breast. Mean time her endoxantheray was stopped and 8 cycles of chemotherapy were recommended then Arimidex (Anastrozole) 1md OD. Her ILD symptoms were flared up. She did not tolerate the severity of attack and passed away within few months. While; going through the investigation we figured out the reason of this sad incidence is the poor channel through which this drug came without proper check – therapeutic drug monitoring, prescription reviewing, biosafety and pharmaceutical evaluation. Furthermore, it is not a single death but representation of so many casualties because of this wrong medications practice. Hence; current health care system needs some more legal, professional and principled restrictions to make sure the safe and correct therapy plans. The clinical legislation, drug rules and medical practice seriously need the attention of judiciary, society and political leadership to assure the safety of precious live.

Keywords: Interstitial lung disease (ILD), Breast cancer, Anastrozole

Introduction

Interstitial Lung Disease (ILD) is a diverse collection of ≥200 lung disorders. It is account for 15% of lung diseases reported to pulmonologist each year[1]. ILD accounts about 15% of lungs diseases reported to pulmonologist every year, these classified together because of their effect on interstitium, alveoli and other compartments of the lung including the bronchioles, trachea, bronchi and the blood vessels, and the pleural membrane of lungs. In general, the most ILD is characterized by respiratory symptoms like chest radiographic abnormalities, typical changes on pulmonary function tests and characteristic macroscopic and microscopic patterns of inflammation & fibrosis.

The lungs of patients show variety of fibrosis & inflammation and characterized by an abnormal structure and excessive inflammatory cells. The causes of ILD can be classified into four categories; diseases that is associated with a condition that affects other parts of the body like autoimmune or collagen vascular disease (sarcodiosis), diseases associated with a specific exposure to an agent that damage the lungs (i.e. bleomycin, tobacco smoke, or agents in the environment that cause hypersensitivity pneumonitis or genetic abnormalities i.e. Hermansky-Pudlak syndrome, Idiopathic diseases[2].ILDs most probably occur in middle-aged or older subjects. Certain interstitial diseases such as sarcoidosis, pulmonary Langerhans cell histiocytosis, and autoimmune-associated lung diseases may develop into young adults, whereas idiopathic pulmonary fibrosis (IPF) mostly occur between the ages of 40 and 70[3,4]. Only a few nations (Germany, Italy, Spain, and Belgium) have collected reliable epidemiological data on ILD In Italy case per100000 is registered each year, while Spain registers 20/100,000. The incidence rate is significantly higher (in the U.S. 81/100,000 in the male population and 67/100,000 in female)[1].IPF constitutes the most frequent ILD. The incidence rate of IPF in the U.S. has reached 7–11/100,000 and in Europe 3–6/100,000. Incidence rate clearly increases with age reaching the level of 175/100,000 for population 75years or above of age[1].Interstitial lung disease is treated with antibiotics like Azithromycin and levofloxacin, corticosteroids like methyl prednisolone, artificial oxygen, immunosuppresents like cyclophosphamide, methotrexate, cyclosporines and N-acetylcysteine.

Health care providers are said to be negligent if they fail to provide the standard care that an expert would give in similar circumstances. If the negligence resulted in injuries or illnesses the health care provider may be liable. If the doctor was clearly wrong, patient can sue him/ her for malpractice[5]. Healthcare professionals are expected to be current in their knowledge of disease diagnoses and treatment to meet a reasonable standard of treatment; depending upon the available facilities for optimum patient's care. The health care professional of the developing part of the worlds may be partially exempted because of the compulsion of adopting the crude methods of care to save the patient's life. According to medical malpractice law, a doctor of Advance counties owes a duty to conduct his practice like a prudent and diligent physician[6]. Standards and regulations for medical malpractice may differ from one country to other and with the jurisdiction within the countries. Medical professionals of developed nations are especially required to maintain professional liability insurance to offset the risk and costs of lawsuits based on local medical malpractice[7]. This report therefore aimed to look at the reasons of clinical errors in developing part of the world. It is not professional revenge, unenthusiastic critics or commercially biased outlook but an optimistic report to encourage the accomplishment of health standards and rational drug usage. Therapeutical drug monitoring, biosafety, pharmaceutical care, prescription review and clinical services carry their meanings in health science. We have to assign the responsibilities to other health caring professionals especially the pharmacists to avoid irrational drug usage.

Case presentation

A 38years female having weight of: 81kg and height: 164cm was presented to the hospital in Lahore. Her socioeconomic history was she belongs to a middle class family. She was presented with chief complaints; paleness, loss of appetite, dyspnea. Lab test: BP 120\80, temperature 100_101°F, SAO2 96%-82%, blood glucose random 110, Rh factor +, HRCT showed NSiP(figure:1), Raynuad's phenomenon, pulmonary function test.

And the final diagnosis of her was Interstitial lung disease.

On basis of her investigation pulmonologist prescribe her Endoxan (cyclophosphamide) 50mg 2 tablets OD (morning), nexum (esomeprazole) 40mg OD, deltacortril enteric coated (methyl Prednisolone) 4 tablets in morning , drat 70 plus D once a week, xynosine nasal spray, citanew 10mg OD. She responds very well to the therapy and her condition was improved gradually.

Two years later scars appear in right breast that showed in her HRCT report. And she was presented to a cancer hospital in Lahore. Labtest:Mammogarm(unilateral),SGPT:30,SGOT:35,TLC:7.0,ESR:15,platelet count:134x103\ul,HB:12.2,neutrophils 64%,lymphocytes 23%,monocytes 7%,eosinophlis 6%. On basis of her lab reports and physical examination she was diagnosed with lymphadenopathy (breast cancer) in right breast. She had a mastectomy after that 8 cycles of chemotherapy. Docetaxel 100mg/m2 (4-6 cycles), cyclophosphamide 600mg/m2 (4-6 cycles), Docetaxel\Carboplatin 155mg\m2 (2cycles). Pulmonary function test, HRCT showed improvement in lung condition (figure:2), SaO2 98%, PEF 300. Then the doctor prescribed her anastrozole for next five years. After 3 month use of anastrozole she was presented to a pulmonologist in the Lahore Chief complaint::dypnea. Lab test: : HRCT showed NSiP(figure:3), SaO2 98% 84%.Pulmonologist comment: Had to stop anstrozole , patient ILD flared up by Chemotherapy. On basis of her diagnosis Palmonologist prescribe her Enteric deltacortil 4OD(Morning), Citanew 10mg OD, Axid neo 40mg OD, Motilium 10mg Bid,

Decok plus OD, Lexotanil(bromazepam) 3mg (At bed), Cavit(levofloxacin) 250mg Bid, Inventive(Dimemorfan) syp Tid ,Oxygen 3_4 liter per min (All the time).The patient died 2 months after initial presentation (Figure 3)

Discussion

Different classes of drugs are used to treat postmanuposal ER-positive breast cancer women in adjuvant therapy for 5 years these includes Selective estrogen receptor modulators (SERMs) like temoxifen, aromatase inhibitors like anastrozole, exemestane and other antiendrogen like fulvestrant.

Anastrozole is 3rd generation aromatase inhibitor ,it is use for the treatment of postmanuposal ER-positive breast cancer women and also use for ER negative breast cancer when it is not respond to temoxifen. Physicians mostly prescribe it anastrozole because it has proven efficacy and tolerability benefits compared with tamoxifen when used as initial adjuvant therapy[8] .but it has many side effects like; angina, thrombocytopenia, hotflashes, bone loss and depression, numbness and weakness of one part of body, pharyngitis, heartattack ,it also cause hypersensitivity reaction in suspected individuals, so proper monitoring is require when patient is treated with aremedix (anastrozole).

Interstitial lung disease is a rare side effect of anastrozole. According to FDA reports there are about 17895 cases were reported of Drug induced interstitial lung disease out of which 0.1% was of aremedix[9].In November 17,2013 it was reported that 13,444 people had side effects by the use of aremedix (anastrozole) out of which 108 people had got ILD by the use of aremedix which is 0.8%.Out of these 108 people 74% patients were using aremedix for the treatment of breast cancer[10]

62 cases were reported on official FDA Adverse Event Reporting Systems (AERS).Out of these 62,48 cases were reported by Physicians,4 by others and 1 by consumer,55 were used it for the treatment of breast cancer. Patient gender distribution is 4.1% in male while and 95.9% in female[11]. Out of these 7 female died due to ILD associated with anastrozole. According to patient age distribution maximum number of patient effected of age 60_69.Maximum number of cases were reported in year 2010_2013.Amoung different countries maximum number of cases were reported from Japan other cultures in which ILD was reported are United State and France[12].One case of anastrozole related interstitial disease was reported on Ask a patient on 4.6.2009. In that case a patient age 71 years with multifocal breast cancer used aremedix (anastrozole) for 3.5 years had got interstitial lungs disease [13]

In Pakistan there is no such case reported about anastrozole before. It would be due to negligence or poor pharmaceutical services or may be due to the fact that ILD is a rare clinical situation.

Conclusion

Poor pharmaceutical services and irrational usage of drug is a major problem of our country. Interstitial lung disease is a rare side effect of anastrozole. My report is emphasis on the fact the good pharmaceutical and clinical care decrease the morbidity and mortality rate associated with rare clinical situations.

Recommendations

1. Enforcement of drugs rules to assure the standard drug monitoring system including prescription review, dose calculation and therapeutic evaluation.
2. Examine and update of the physicians for their executed procedures, scientific techniques, chemotherapy protocols, professional skills and clinical expertise.
3. Maintenance of the threat of lawsuit is an excellent reason of quality services. If may become more effective if helped by insurance coverage. The insurer should be notified. Notice is a requirement of all policies and it may authorize a quick settlement.
4. Make sure the availability of clinical pharmaceutical services round the clock. The pharmacist must have to collect the medical, social, personal and professional data on patient to figure out any possible potential health hazard.
5. Implementation of the six major contributing elements of hospital pharmacy section designed by the international pharmaceutical federation (FIP) with the collaboration of World Health Organization, UNESCO, World Health Professions Alliance, Regional Pharmaceutical Forums and all other partners[14]
6. The patient and/ guardian should be briefed about the illness, treatment protocol, and possible outcomes if professional ethics have no restriction to do so. It may also help to instigate the procedure to uncover the patient's complaints.
7. Development of a process of handling the patient complaints; that may help to create a long-term effect of reducing malpractice risks. Most patients are willing to forgive occasional annoyances or disappointments if they perceive that medical professionals and the office staff care about their needs and are trying to satisfy them. Therefore; the verbal, non-written policy and unofficial procedure may help to cope with the situation and develop professional understanding.
8. The physician should try to keep the patients well treated and happy. He should be vigilant about the inevitable complaints and strategy to tackle. Furthermore; in staff meetings the problems and complaints should be discussed for future benefit.
9. Any kind of patient's letter, phone call, email or text message should be bothered and invite for a free consultation. He should be replied promptly with an expression of taking good care of his case that will mitigate the grumbles and improve level of satisfaction.
10. The patient should be addressed directly in case of clinical grievance. The physician has to involve him more seriously to assure the quality of care concerns. The bad result is not necessarily the result of any human failures/ error.
11. The problems related to the irregular visit, nonprofessional behavior, inadequate diagnostic facilities and non healthy condition in the hospital setting can only be resolved by designing certain rules and regulations.

Acknowledgement

The author wishes to acknowledge Mr., Director, Dr. Sajjid Bashir(Dean of Faculty of Pharmacy, University of Sargodha, Pakistan.

References

1. Interstitial lung diseases: an epidemiological overview. Eur Respir J 2001; 32:2s.
2. American Thoracic Society, European Respiratory Society. June 2001. Am J Respir Crit Care Med 2002; 165:277–304.
3. Coultas DB *et al*. The epidemiology of interstitial lung diseases. Am J Respir Crit Care Med 1994; 150:967–972.
4. Olson AL *et al*. Mortality from pulmonary fibrosis increased in the United States from 1992 to 2003. Am J Respir Crit Care Med 2007; 176:277–284.
5. Doctor felt babies were suffering. *BBC News*. 2007- 07-09. Retrieved 2010-05-21.
6. http://www.lawmedmal.ca/medical_malpractice_law.htm
7. BBC article on lethal injection http://news.bbc.co.uk/2/hi/americas/7350982.stm
8. The Canadian Bar Association, British Colombia Branch,10th Floor, 845 Cambie Street, Vancouver, BC V6B 5T3http://www.cba.org/bc/public_media/health/420.aspx

9. http://medsfacts.com/study-ARIMIDEX-causing INTERSTITIAL%20LUNG%20DISEASE.php
10. http://www.ehealthme.com/ds/arimidex/interstitial+lung +disease
11. http://www.drugcite.com/indi/?q=ARIMIDEX&s=&a=&i=I NTERSTITIAL+LUNG+DISEASE#showRxAdverseEvents
12. http://www.druginformer.com/search/side_effect_details/ arimidex/interstitial%20lung%20disease.ml
13. http://www.askapatient.com/viewrating.asp?drug=20541& name=ARIMIDEX&page=9&PerPage=60
14. http://www.fip.org/hospital_pharmacy

	PRE Trial data			POST bronchodilation with salbutamol			
parameters	Pred	PRE	%Pred	POST	%Perd	%Chg	PRE#1
Forced Vital Capacity							
Best values from all loops							
FVC (L)	3.15	1.04	33	1.05	33	1	1.04
FEV1(L)	2.66	1.00	38	1.01	38	1	1.00
FEV1\FVC(%)	84.6	96.2	114	96.2	114	0	96.2
PEF(L\S)	6.43	2.91	45	4.00	62	37	2.91
Values from best loops							
FEF2575	3.43	2.00	58	2.24	65	12	2.00
FEF25	6.05	2.89	48	4.00	66	38	2.89
FEF50	3.99	2.37	59	2.56	64	8	2.37
FEF75	1.78	0.96	54	0.92	52	-4	0.96
FIVC	3.15	0.93	30	0.86	27	-8	0.93
FIV1	2.66	0.93	35	0.86	32	-8	0.93
FIV1\FIVC	84.6	100.0	118	100.0	118	0	100.0
ELA(YEARS)	35	132		132	377	0	132

Table 1. Pulmonary function test(initial)

	PRE Trial data			POST bronchodilation with salbutamol			
parameters	Pred	PRE	%Pred	POST	%Perd	%Chg	PRE#1
Forced Vital Capacity							
Best values from all loops							
FVC (L)	3.04	1.05	35	1.13	37	8	1.05
FEV1(L)	2.57	1.00	39	1.07	42	7	1.00
FEV1\FVC(%)	84.7	95.2	112	94.7	112	-1	95.2
PEF(L\S)	6.28	4.27	68	4.49	72	5	4.27
Values from best loops							
FEF2575	3.31	2.07	63	2.09	63	1	2.07
FEF25	5.91	4.19	71	4.46	75	6	4.19
FEF50	3.88	2.27	59	2.49	64	10	2.27
FEF75	1.70	0.79	47	0.80	47	1	0.79
FIVC	3.04	1.13	37	1.09	36	-4	1.13
FIV1	2.57	1.13	44	1.09	42	-4	1.13
FIV1\FIVC	84.7	100	118	100	118	0	100
ELA(YEARS)	37	129		125	338	-3	129

Table 2. Pulmonary function test (improved)

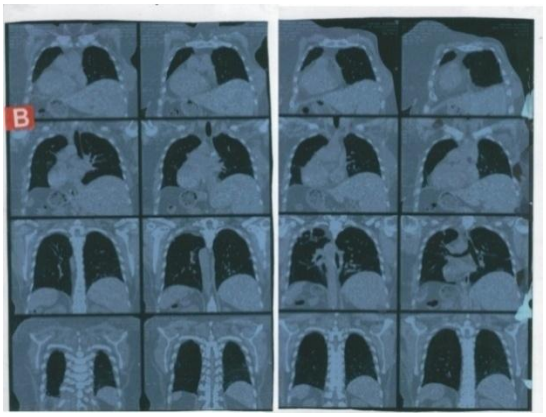

Fig. 1. HRCT

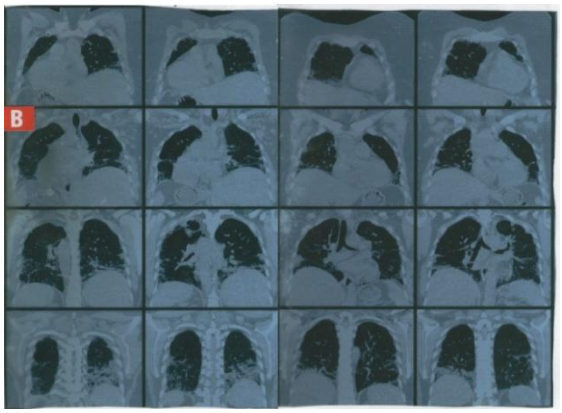

Fig. 2. HRCT

	PRE Trial data			POST bronchodilation with salbutamol			
parameters	Pred	PRE	%Pred	POST	%Perd	%Chg	PRE#1
Forced Vital Capacity							
Best values from all loops							
FVC (L)	3.04	0.56	18	0.58	19	4	0.56
FEV1(L)	2.57	0.56	22	0.587	23	4	0.56
FEV1\FVC(%)	84.7	100	118	100.0	118	0	100
PEF(L\S)	6.28	2.70	43	3.54	56	31	2.70
Values from best loops							
FEF2575	3.31	2.26	68	2.52	76	12	2.26
FEF25	5.59	2.49	42	3.51	59	41	2.49
FEF50	3.88	2.41	62	2.69	69	12	2.41
FEF75	1.70	0.93	55	1.00	59	8	0.93
FIVC	3.04			0.67	22		
FIV1	2.57			0.67	26		
FIV1\FIVC	84.7	0.0	0	100.0	118		0.0
ELA(YEARS)	37	154		153	414	-1	154

Table 3. Pulmonary function test (after drug reaction)

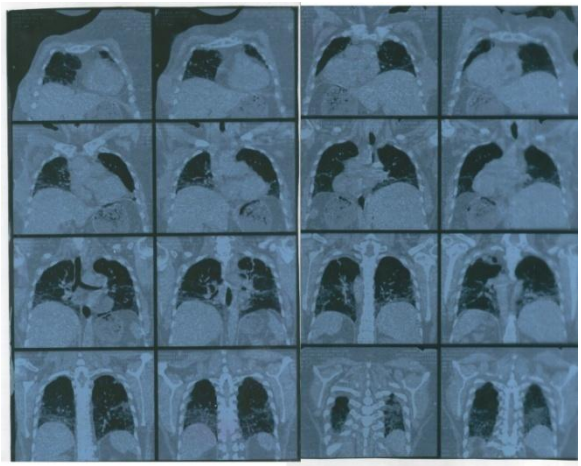

Fig. 3. HRCT