CASE REPORT

Radiation Recall; A Paediatric Case Report From University Teaching Hospital, Lusaka

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ABSTRACT

Radiation Recall Dermatitis (RRD) is an acute inflammatory reaction that develops within an area of previous irradiation, occurring after administering a chemotherapeutic agent. We present the case of a 3-year-old Zambian girl with a nephroblastoma who developed radiation recall after the administration of dactinomycin, doxorubicin and vincristine. Our case attempts to highlight the importance of this rare condition. Given that radiotherapy and chemotherapy have such a close relationship in a multitude of cancers we feel it increasingly important to further understand this phenomenon and specifically its associations with certain drugs and susceptible individuals. To the best of our knowledge this is the first documented paediatric case of radiation recall from Zambia.

BACKGROUND

Radiation recall dermatitis was first described in 1958 when it was observed with dactinomycin [3]. As most information comes from case reports pertaining to adults, it is not possible to determine the true incidence or prevalence

The most frequent site of RRD is the skin but other reported involved organs include mucous membranes, lungs, oesophagus, gastrointestinal tract, central nervous system, bladder, and heart [1]. A number of different drugs have been identified to cause it (see table 1), the most common being the cytotoxic antibiotics (dactinomycin, doxorubicin, daunorubicin, and bleomycin), the taxanes (paclitaxel. docetaxel), and methotrexate [1]. Due to limited evidence and lack of knowledge regarding aetiology it is not possible to determine which patients will react to which drugs. 'There are no identifiable characteristics of drugs, that cause radiation recall, and thus it must be kept in mind with the use of any drug after radiotherapy including new drug classes' [4]

Table 1

Drugs Causing Radiation Recall Dermatitis	
Drug	
5-fluorouracil	Hydroxycarbamide
Bleomycin	Hydroxyurea
Cytarabine	Interferon-α-2b
Cyclophosphamide	Lomustine
Dacarbazine	Melphalan
Dactinomycin	Mercaptopurine
Daunarubicin	Methotrexate
Doxorubicin	Oxaliplatin
Edatrexate	Paclitaxel
Etoposide	Tamoxifen
Gemcitabine	

The three manifestations of radiation recall are:

1. A mild reaction consisting of erythema, oedema and dry desquamation
2. A moderate reaction with moist desquamation, vesiculation, blister formation and erosion
3. Severe necrotic ulcerative reactions that could result in skin hypopigmentation [1]

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It has been proposed that the more-severe skin reactions, occur more frequently when the period between radiation and the recall-triggering drug is shorter [2]. Our patient presented thirty days post radiation and eight days post chemotherapy. However radiation recall dermatitis may present with a latency period of months to years [3].

CASE PRESENTATION

A three year old Zambian girl with no significant past medical history and from an affluent background, presented in April 2011 to the paediatric department at the University Teaching Hospital, Lusaka. She had a ten day history of a right sided abdominal mass, on a background of reduced appetite and non specific weight loss. Ultrasound confirmed the presence of a capsulated abdominal mass and a prompt subsequent intravenous pyelogram indicated a large right-sided hyperdense lesion, approximately 12.5 x 10cm with some mass effect.

She went on to have an Magnetic Resonance Imaging (MRI), to establish the aetiology of the mass. A subsequent Vanillyl Mandelic Acid (VMA) test diagnosed a nephroblastoma, which was later confirmed histologically. The nephroblastoma chemotherapy protocol was swiftly commenced, ten days after initial presentation. This consisted of: dactinomycin, vincristine and doxyrubicin. She tolerated this well and after six cycles a repeat MRI concluded that the mass had reduced in size. A successful right nephrectomy was undertaken six weeks after initial presentation.

There were no post operative complications and three weeks later she was re-commenced on chemotherapy solely in the form of vincristine. After a total of ten cycles of chemotherapy, radiotherapy was commenced and finished three weeks later. The subsequent second phase of chemotherapy began with the re-administration of all three original cytotoxic agents.

Three days later she presented with fever, reduced appetite and drowsiness. Broad spectrum antibiotics were administered as a precautionary measure. Despite this, her clinical state was such that chemotherapy was able to continue.

On day eight there was a significant turning point; an erythematous patch of dry desquamation on the right side of the back was noted correlating with the site of radiation. The patient was treated symptomatically with oral steroids and antihistamines. After consulting the radio-oncologist, a working diagnosis of radiation recall was reached. This was largely due to the specific location (within the irradiated area), timing (after chemotherapy) and presentation (absence of any other cause or pre-existing skin pathology) of the dermatitis in this case. The patch of dry desquamation failed to respond to treatment and rapidly transformed into an area of ulcerative necrotic tissue.

Over the course of the next few weeks, her clinical state decompensated. She developed overwhelming sepsis secondary to immunosuppression induced by chemotherapy and radiotherapy. It was thought by the medical team that the area of necrosis was a possible contributing factor to her sepsis.

Unfortunately due to a combination of immunosuppression, sepsis and hepatorenal failure the patient died six months after her initial presentation.

DIFFERENTIAL DIAGNOSIS

Radiation recall dermatitis could show clinical findings similar to those of acute radiation induced dermatitis [1].

Areas of skin irritation or infection can also become further inflamed during the administration of a chemotherapeutic agent thereby making it difficult to differentiate between radiation recall dermatitis and acute radiation induced dermatitis, which is related directly to radiotherapy [1].

In our case, the initial medical report indicates that the patient had no skin abnormalities prior to commencing radiotherapy. She presented with features of a mild radiation enhancement reaction, crucially eight days post adjuvant chemotherapy. Both the location of the dermatitis and the natural history of when it occurred is in keeping with a diagnosis of radiation recall.

Camidge and Price have further defined the clinical entity and have made a clear separation between

radiation induced dermatitis and radiation recall dermatitis. They suggest designating any reaction occurring within seven days after administration of drugs as sensitisation and not as radiation recall dermatitis [2]. In our case the interval was eight days post chemotherapy and thirty days post radiotherapy. This can, by the above definition, be called radiation recall dermatitis. Although the interval of eight days can be considered relatively short, much longer intervals of up to 25 years have been described [6].

TREATMENT

There are no proven interventions to relieve symptoms or to enhance recuperation. Once the radiation recall dermatitis has occurred almost all reports advice to discontinue the triggering drug [2]. However, a re-challenge does not always result in the occurrence of the skin reactions [2].

DISCUSSION

Dactinomycin and doxorubicin were the most likely agents to have caused the radiation recall in our case [5]. From literature that was reviewed we found no other reported cases involving dactinomycin, doxorubicin and vincristine in the same treatment regime causing radiation recall. Most reports of radiation recall are in response to administration of a single chemotherapeutic agent. However, there is no evidence to suggest that combination chemotherapy either increases or decreases the risk of radiation recall compared with monotherapy [2].

Approximately fifteen cases of doxorubicin induced radiation recall dermatitis have been cited [7]. One such case demonstrates quite clearly the crucial relationship between radiotherapy and the administration of the offending chemotherapeutic agent:

A 44 year old female patient with a large grade three infiltrating ductal carcinoma and local metastases commenced treatment for breast cancer. Six weeks after breast conserving surgery she was irradiated to the left breast, axilla and internal mammary chain. Exactly fourteen days after completion of radiotherapy she started her adjuvant chemotherapy; taxotere, doxorubicin and cyclophosphamide (TAC). On day four after administration of TAC chemotherapy, the irradiated skin started to show an erythema with a purplish aspect. Since the indication of adjuvant chemotherapy was considered to be crucial, she was encouraged to continue without doxorubicin. On day 22 the second chemotherapy course was administered consisting of TC and the skin reaction did not re-occur. Subsequent courses could be administered without reappearance of the recall phenomena [5].

Despite the fact that the first documented case of radiation recall involved dactinomycin we were unable to find any current evidence to support how strong this link is. The same can be said with regards to vincristine.

It is difficult to appreciate the total contribution that the radiation recall dermatitis made in the days leading up to this patient's death. It was clear that severe sepsis was the major contributing factor to mortality. However, we were unable to establish the exact site of this or a specific causative organism. We believe however that regardless of its direct role in this patient's mortality, the diagnosis of radiation recall should not be underplayed.

CONCLUSION

In Zambia, dactinomycin, doxorubicin and vincristine are commonly used in the treatment of nephroblastoma. It would therefore be pertinent that physicians treating patients with these drugs need to be aware of the potential of radiation recall dermatitis so as to aid early diagnosis and initiate appropriate management. The sporadic and unpredictable nature of this condition makes management challenging. More research in this area needs to be carried out to better recognise susceptible individuals thereby preventing this reaction.

INFORMED CONSENT

Obtained from parents

COMPETING INTEREST

None

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