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Management of toxicities from Immunotherapy in cancer patients

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ABSTRACT

Background: Monoclonal antibodies targeting cytotoxic T lymphocyte-associated antigen 4 (CTLA4) and the programmed death-1 receptor (PD-1) are increasingly being used in the treatment of cancer. However , management and recognition of toxicities (Immune related adverse events) have been a problem for junior doctors in Ed and on acute medical take. irAEs could be potentially life threatening if not anticipated and managed appropriately.

Aim: Improving recognition, documentation and early management of toxicities from immunotherapy.

Methods: Data was collected retrospectively for the period of June to September 2019 (4 months period). Relevant information was extracted from Ice, EDMS , Symphony, discharge summaries and clinical letters.

Results: 34% patients admitted with diarrhoea, 9% were admitted with mucostis and 8% were admitted with rash and likely hypophysitis. One case of OHCA was reported whereas in 25 % cases there was no documentation and also grade of toxicity was not documented in the initial clerking notes. In most of the cases, steroids were started either on the same day or either within 24 hours by the AOS team.

Conclusion: Improvement needed in documenting and assessing grade of toxicity as it impacts the treatment. Also, education sessions needed to familiarise juniors in ED and on acute medical take about the management of irAEs and how to access guidelines (which are currently on intranet). We will assess again in 3 months' time for improvement.

PROBLEM

The increasing success of immunotherapy in cancer patients, on one hand has increased the survival in cancer patients, however, on the other hand, their use is associated with adverse effects on multi organs [1][2]. The immune related adverse events can involve any organ and can mimic autoimmune conditions. For example, involvement of liver can cause hepatitis and skin involvement can cause toxic epidermal necrolysis [3][4]. This leads us to the need of a multispecialty approach in treating such adverse effects, which otherwise if not anticipated and managed properly in time could be potentially life threatening[5]. Recognition and management of the toxicities (Immune related adverse events IrAEs) have been a problem for the junior doctors in the ED (Emergency department) and on the acute medical take. It was identified that there was a delay in recognition, documentation and hence treating such patients when they were presented in ED specially OOH (out of hours). A discussion pre teaching session and the feedback revealed that this was due to the combination of factors including reluctancy in starting high dose steroids, lack of awareness of as to where the relevant guidelines could be found and lack of knowledge about the immunotherapy and hence treatment. The proposed pathway for any patient with suspected adverse effects secondary to immunotherapy in the DGH has been shown in figure 2:

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AIM

The aim of the project was to collect data and information about how IrAEs were managed in the ED and on the medical take before they were referred to the AOS (Acute oncology service), and based on that educate the juniors around this subject, to improve the recognition, initiation of appropriate treatment without delay and documentation of the grade of the immune related adverse effects.

METHODS

Data about the initial presenting symptoms and the treatment these patients received initially was collected retrospectively for the period of June to September 2019 (4 months period). Relevant information was extracted from the hospital intranet applications - ICE, EDMS, Symphony, discharge summaries and clinical letters. Education and a reminder of the existing pathway of referrals were the main interventions to improve the outcome and adherence.

RESULTS

Over a period of four months, a total of 14 cases were assessed 34% were admitted with diarrhea, 9% with mucositis and 8% with rash and likely hypophysitis. One case of out of hospital cardiac arrest was reported. Overall, in 25% cases there was neither documentation nor the grade of toxicity was documented in the initial clerking notes.

Also, in almost 99% cases, the steroids were started by the Acute Oncology team and not on admission by the admitting teams (fig 1). As the initial discussion pre teaching session revealed, the reasons behind medical and ED teams not starting steroids were the reluctancy and the lack of education around this subject.

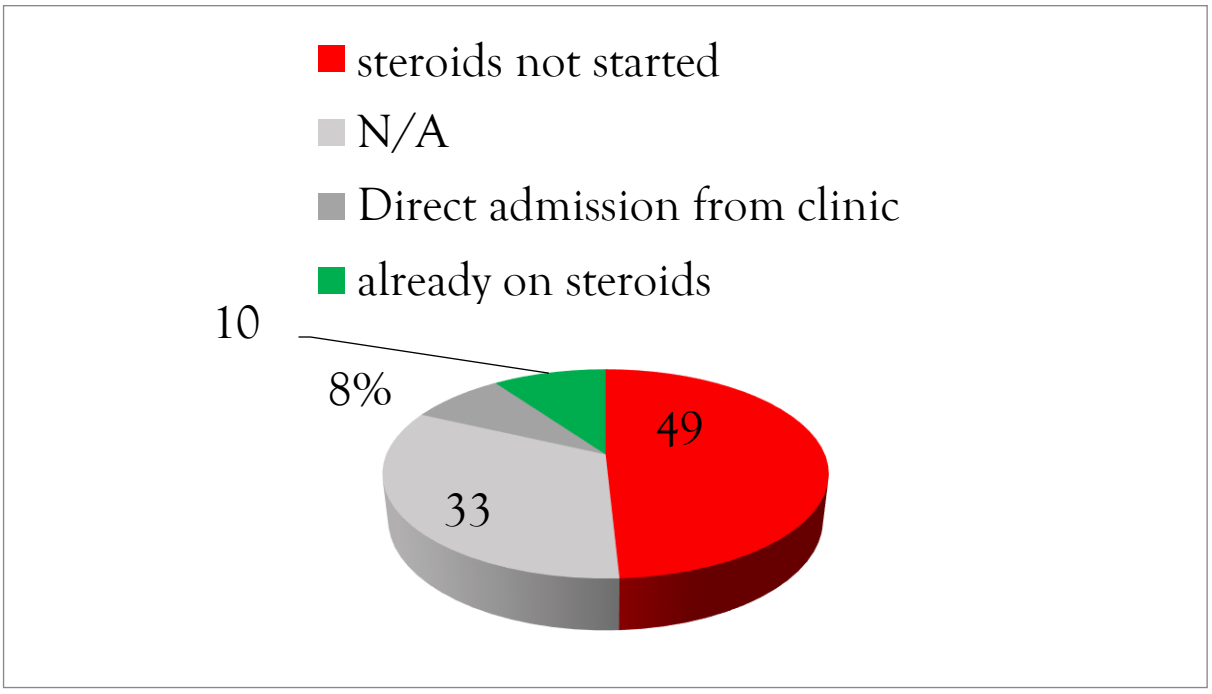

Fig 1: Pie chart demonstrating the initiation/prescription of steroids in the ED in patients admitted to the hospital with IrAEs.

DISCUSSION

As evidenced from the data, improvement was needed in documenting and assessing grade of toxicity while assessing such patients, as it impacts the treatment.

To address this, education sessions were delivered by the AOS team to familiarize junior doctors in ED and on acute medical take about the management of irAEs and how to access guidelines on the intranet.

Though official PDSA cycle results are being compiled, however, a glance at the data showed that the educational sessions have improved the knowledge and awareness around this subject.

General guidelines on management of toxicities from Immunotherapy
Discuss with the senior if unsure about the management
Admit the patient with grade 3-4 toxicity and consider holding the immunotherapy
Manage the patient according to the local guidelines
Liaise with the relevant specialty (like dermatology in case of rash) in addition to acute oncology service
Referral to AOS (Acute Oncology Service)
Start high dose steroids (methylprednisolone 1-2mg/kg or Prednisolone 1-2mg/kg)
Discuss with the oncologist if no improvement in 48-72 hours post starting steroids

Fig 2: Proposed Pathway for patients with suspected toxicity from immunotherapy

LESSONS AND LIMITATIONS

This project was conducted in a DGH and continues teaching sessions and reminders in the form of posters are needed to sustain the change, mainly due to the diverse range of presentation of symptoms.

CONCLUSIONS

Toxicity secondary to immunotherapy can be life threatening. Lack of knowledge among junior doctors leads to unnecessary delays in commencing steroids. Robust steps need to be taken to address this in form of educational sessions by AOS team.

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DECLARATION OF INTEREST

Nothing to declare.

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