INTRODUCTION/BACKGROUND

Denosumab is a monoclonal antibody directed against RANKL which is commonly used to treat osteoporosis. Denosumab has been associated with increased risk of serious infections of the abdomen and urinary tract, as well as increased risk of skin infections such as cellulitis and erysipelas [1,2].

Malakoplakia is a rare granulomatous inflammatory condition most commonly affecting the urinary tract that is associated with immunosuppression and defects in macrophage destruction of bacteria. Malakoplakia is associated with acquired immunosuppression [3].

The RANK-RANKL system is a pathway involved in the immune cells and other associated cell lines. This pathway has been well studied for its role in osteoclast differentiation which was implications in osteoporosis [4]. However, it is also important in immune regulatory systems. RANKL has a role in dendritic cell survival and downstream T-cell regulation [5].

CASE SUMMARY

We present a case of a 67-year-old woman on denosumab who developed malakoplakia of the bladder during her treatment course. She was being treated for osteoporosis with denosumab since 2015. She presented to her urologist since 2015. She presented to her urologist with symptoms and referred to urology if there is not a clear etiology.

Patient's on denosumab should be screened for lower urinary tract symptoms and referred to urology if there is not a clear etiology. Alternative treatments should be considered in those with recurrent UTIs or significant lower urinary tract symptoms.

DISCUSSION

While denosumab may increase infection risk, there are no studies showing increased prevalence of malakoplakia in those taking denosumab. This may be a late manifestation of denosumab treatment or an indicator of immunosuppression in those on denosumab.

As malakoplakia is associated with immunosuppression and macrophage defects, which have not been described in those on denosumab therapy, this may be an indicator of greater suppression than previously thought.

Studies on the effect of RANKL inhibitors on immunity are somewhat conflicting. Immunologic research papers describe the RANK-RANKL pathway as either promoting or suppressing immunity based upon the specific phase of the immunity cycle it is activated [10]. RANKL promotes dendritic cell survival.

Dendritic cells play a significant role in the innate immune system and immune regulation in the epithelium [11]. RANKL inhibition may lead to reduced dendritic cell survival and therefore altered epithelial immunity.

CONCLUSIONS

Patients taking denosumab have an increased risk of cellulitis, serious infections and UTIs which may include malakoplakia.

REFERENCES