

## Two cases of renal cell cancer during immunobiologic therapy for psoriasis\*

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**Abstract:** Immunobiologic therapy is indicated for severe forms of psoriasis, resistant to conventional therapy. There is growing concern about their safety profile and possible association with cancer development. This article documents two cases of renal cell cancer during treatment with biologic therapy, reviewing what is described in the literature. The risk of solid tumors as a complication of using TNF-alpha inhibitors is controversial. No conclusion can be drawn from the data in the literature, however, we believe that special attention should be given to those with known risk factors for a specific neoplasm.

**Keywords:** Biological therapy; Kidney neoplasms; Psoriasis

Psoriasis is a chronic autoimmune disease that affects the skin and joints, with worldwide prevalence ranging from 0.8 to 4.6%.<sup>1</sup> A large number of topical and systemic treatments are available, and immunobiologic therapy is indicated for moderate to severe resistant forms, or individuals for whom conventional therapy is contraindicated. However, there is a growing concern about the safety profile, mainly due to the possible association of these drugs with an increased incidence of neoplasia. This article documents two cases of renal cell cancer during treatment with biologic therapy, reviewing the literature so far.

The first case concerns a 41-year-old man with eleven years of severe psoriasis and psoriatic arthritis (polyarticular and axial involvement). His level on the Psoriasis Area and Severity Index (PASI) remained at 28.9 despite taking methotrexate (MTX). Infliximab 4mg/kg was thus added to existing therapy and he responded excellently. After a year of treatment, the calculated PASI was 1.8. At one hundred and eight weeks of infliximab, hepatitis was diagnosed due to the development of jaundice and elevated transaminase levels. An abdominal ultrasound was requested, which revealed a mass in the right kidney. After a urology evaluation, a total nephrectomy was performed with a diagnosis of clear cell renal carcinoma

by histopathological analysis. The surgery was curative and administration of leflunomide 10mg/day stabilized joint symptoms and partially controlled the cutaneous lesions.

The following report concerns a 66 year-old man with a 40-year history of psoriasis. He had already used MTX and was undergoing psoralen in addition to UVA light therapy (PUVA) treatment twice a week, and taking acitretin 30mg once a day. Despite the instituted therapy, new cutaneous lesions and joint symptoms appeared, leading consequently to the initiation of etanercept at a dose of 50mg per week. He achieved disease control with resolution of the joint symptoms and a decline in PASI of more than 90%. After two hundred and eighteen weeks of therapy, prostatic symptoms led to an abdominal ultrasonography. In this case, a renal mass was also found and the patient underwent a total nephrectomy, whose histopathological examination revealed papillary renal carcinoma. Surgery was also curative, and the patient kept the disease under control with 30mg/day of acitretin.

Renal cell carcinoma accounts for 3% of all malignancies, is twice as common in men and the age group 50-70 years is the most affected.<sup>2</sup> The most common histologic type is clear cell carcinoma (75-85%)

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followed by papillary (10-15%), chromophobe (5-10%), oncocytic (3-7%) and collecting duct (<1%).<sup>3</sup> Since it is a silent cancer, the increased availability and improvement of imaging methods have led to a large increase in the percentage of incidental renal tumors, with 50% classified as incidentalomas.<sup>4</sup>

Data on the risk of solid tumors as a complication of using TNF $\alpha$  (Tumor necrosis factor alpha) inhibitors are controversial. A study in Sweden with three cohorts found that the risk of solid malignancies in patients with rheumatoid arthritis treated with TNF $\alpha$  inhibitors is not greater than what would be expected with the disease alone.<sup>5</sup> A meta-analysis of 63 studies, including a total of 29,423 patients, found no significant risk among those undergoing biologic therapy, compared with disease-modifying drugs or placebo, with a follow-up of at least 24 weeks.<sup>6</sup> However, a double-blind, randomized study, showed increased risk of solid tumors in patients with Wegener's granulomatosis treated with TNF $\alpha$  inhibitors and cyclophosphamide, compared with those treated only with cyclophosphamide.<sup>7</sup> Do TNF $\alpha$  inhibitors increase the chance of solid tumors, such as renal neoplasia? Or have they been overdiagnosed due to advances in imaging methods, leading to bias in studies?

In the specific case of renal cell carcinoma, few reports showed renal neoplasia in patients undergo-

ing immunobiologic therapy. Some authors studied the benefit of TNF $\alpha$  inhibitors as an adjunctive therapy in treating these tumors, based on the fact that TNF $\alpha$  receptors were found in neoplastic renal cells.<sup>8</sup> We have found evidence in the literature that patients with psoriasis have an increased incidence of lymphoproliferative disorders, particularly Hodgkin's lymphoma and cutaneous T-cell lymphoma.<sup>9</sup> There is also a higher risk of solid tumors, and associated characteristics include the use of oral medication (gravity indicators) and long duration of disease ( $\geq 4$  years).<sup>10</sup>

TNF $\alpha$  inhibitors are associated with potentially serious adverse effects. However, these risks must be interpreted in the context of the potential benefits associated with such products.

The adverse effects of conventional treatments, including the risk of inducing malignancy, are also significant in most cases. Thus, the decision to use a TNF inhibitor should be individual, based on the specific clinical characteristics and specific risk profile of a particular patient.

With respect to the patients described above, we cannot draw conclusions from the data found in the literature regarding the development of renal cancer with the instituted therapy. However, we believe that special attention should be given to those with known risk factors for a specific neoplasm, who use these medications. □

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