

Case Report

Diagnosis of a plasmoblastic lymphoma of the mandible after renal transplantation: a case report

Inès Legeard^{*}, Marc-Antoine Chevrollier, Gérard Bader

Service d'odontologie, chirurgie orale et implantologie, CHU de Rennes, rue Henri le Guilloux, 35000 Rennes, France

(Received: 4 January 2021, accepted: 1 September 2021)

Keywords:
Post-transplant
lymphoproliferation /
Epstein-Barr virus /
oral cavity

Abstract – Introduction: Post-transplant lymphoproliferations (PTL) are a severe complication of solid organ transplants. Their locations can be extra-nodal. **Observation:** The diagnosis and management of a non-Hodgkin's plasmablastic lymphoma of mandibular localization affecting a 66-year-old kidney transplanted patient are reported here. **Comment:** The main risk factors for non-Hodgkin lymphoma are immunosuppression and infection with Epstein-Barr virus. Clinical and radiographic examinations, which are not specific, must be supplemented by a histological examination. Treatment which is not consensual will most often consist of a reduction in immunosuppression coupled with chemotherapy. **Conclusion:** Despite a constant evolution in the incidence and clinical picture of post-transplant lymphomas, the role of the dentist remains essential in the early detection of lesions.

Introduction

According to the new classification from the World Health Organization, post-transplantation lymphoproliferative (PTL) syndromes cover a heterogeneous set of benign or malignant pathologies, including lymphoma, occurring in a context of post-transplantation immunosuppression due to quantitative or qualitative T lymphocyte damage [1]. They represent a severe complication occurring in patients with solid organ transplants such as kidneys.

Non-Hodgkin lymphoma (NHL) are usually lymph node, but 20–30% of the sites are extra-nodal [2], particularly affecting the oral cavity. A case of mandibular plasmablastic lymphoproliferative syndrome in an Epstein-Barr virus (EBV) positive patient is presented here.

Since 2011, only one case of oral cavity plasmablastic lymphoma occurring after solid organ transplantation has been documented.

Observation

A 66-year-old man presented to the dental emergency department following the appearance of buccal and lingual swelling in the lower right mandibular molar region evolving over the past two weeks. This patient had a kidney transplant

4 years ago. His treatment was tacrolimus, cortisone and catapressan.

Intraoral examination revealed vestibular and lingual gingival hypertrophy ranging from 44 to 47 (increased around 46, mesioversed) the mucosa was erythematous and ulcerated (Fig. 1). This lesion was painless on palpation. The teeth facing the lesion were vital. Neurological examination of the right alveolar nerve territory was normal.

The orthopantomogram showed a periodontal pocket mesial to tooth 46 (Fig. 2). The cone-beam was unremarkable (Fig. 3).

Due to the suspicious macroscopic appearance of the lesion, a biopsy was performed at the site. Histological analysis was in favor of a post-transplant monomorphic lymphoproliferative syndrome. The immunohistochemistry specified a plasmablastic-type lymphoma.

The patient was referred to the hematology department for an extension assessment. The whole body CT scan did not show any other localization.

PCR was positive for EBV with 132,000 copies of the viral genome.

The strictly medical management consisted of treatment with 2 courses of R-CHOP (R-CHOP: rituximab, cyclophosphamide, vincristine, doxorubicin, methylprednisolone) associated with a reduction of the dosage of tacrolimus, in order to reduce immunosuppression induced by this treatment (from 3 mg a day to 2 mg a day).

* Correspondence: legeard.ines@gmail.com



Fig. 1. Intraoral picture: vestibular and lingual gingival hypertrophy ranging from 44 to 47.



Fig. 2. Orthopantomogram: periodontal pocket mesial to tooth 46.

The response to treatment was favorable and complete remission was obtained after this treatment.

Comments

In terminal chronic kidney failure, kidney transplantation is currently the standard treatment ensuring better patient survival.

However, immunosuppressive anti-rejection therapy greatly increases the risk of developing infections and neoplasms. Thus, cancers occur in 30% of cases and represent the major cause of death in kidney transplant patients. After skin cancer, malignant lymphoid proliferation is the most common [3].

The new classification from the World Health Organization groups NHL, myeloma and Hodgkin lymphoma after transplant into a category called post-transplant monomorphic lymphoproliferations [1].

NHL represents, after squamous cell carcinoma, the second cancer of the head and neck region, accounting for 2.6% of the lesions encountered [4]. After renal transplantation, its incidence is 0.4% at one year and 1% at five years [5].

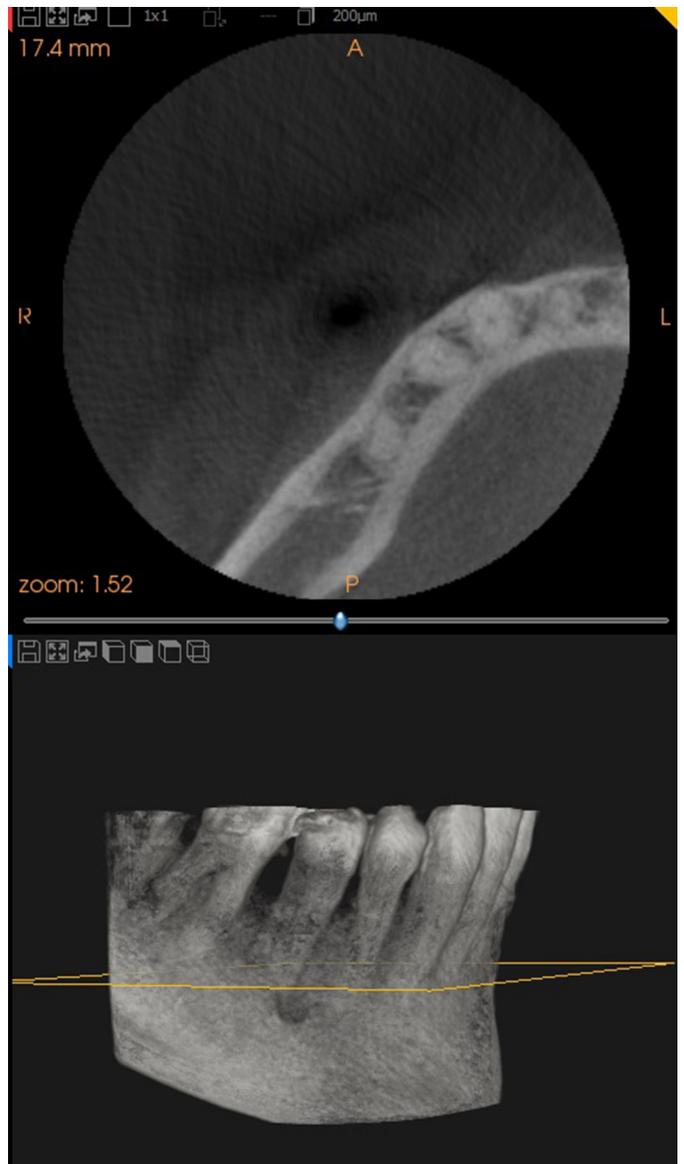


Fig. 3. Computed tomography focus on sector 4: unremarkable.

The main risk factors for developing PTL are infection with EBV and immunosuppression [2]. In fact, in a transplant patient, the antiviral defenses are impaired mainly by the immunosuppressive treatment which decreases the cytotoxic T response, responsible for the fight against cells infected with EBV.

EBV contamination plays a major role in this oncogenic process. This lymphotropic virus infects over 90% of the general population. Unlike an immunocompetent patient, the transplant patient does not have sufficient cellular immunity to control his primary infection and periodic reactivations of EBV. An EBV-negative patient (8% of the general population) receiving a transplant from an EBV-positive donor has a high risk of developing post-transplant lymphoma: 11.5% after primary infection and 3.6% after reactivation [6].

The locations of NHL are varied. The main sites are the graft itself (12%), digestive (25%), cerebral (14%), isolated ganglia (13%) but also cutaneous, ENT and oral [5]. In the oral sphere, they can involve the tongue, the gingiva, the hard palate, the jaws, the palatine and lingual tonsils, and more generally all the structures constituting the Waldeyer's ring [7].

Among NHL, the most frequently encountered histological type is that with large B cells [8].

Plasmablastic lymphoma (PBL) is a rare aggressive variant of large B cell lymphoma defined as a proliferation of large neoplastic plasmoblasts [9].

PBLs in immunocompromised patients, like transplanted [10] or HIV-positive patients, show a predilection for the oral cavity, although extra-oral involvement is found [11]. They are predominant in male and more frequently affect the adult population, with a median age of presentation being in the fourth decade [12,13].

PBLs also develop in immunocompetent patients, usually already over 60 years old by the time of showing.

A third of these PBLs' occurrences are in absence of EBV+ [14].

Clinically, in our patient, the swelling was not painful but we can also find bone or dental pain when lymphoid cells infiltrate the dental pulp. The clinical picture can also find dental mobility or loss, pathological fractures [1,15] or even paresthesia of the inferior alveolar nerve secondary to its compression or infiltration. A general sign such as fever, night sweats or weight loss may also appear [12].

Radiographic examination is not specific in the initial stage. At a more advanced stage, we may find osteolysis, periosteal thickening, periodontal enlargement or enlargement of the mandibular canal [1,16].

Due to the absence of radio-clinical specificity, several diagnostic hypotheses can be raised: either benign (periodontal disease, pericoronitis, periodontal abscess), or malignant (multiple myeloma [12], primary bone carcinoma, bone metastasis, osteomyelitis).

The diagnosis must be confirmed by histological and immunohistochemical analysis.

The detection of EBV is conventionally carried out by in situ hybridization (search for RNA not coding for EBV) or by immunohistochemistry (detection of EBV Ag or proteins expressed by EBV).

In our patient, this test was positive and confirmed by PCR test with a high replication rate, indicating a recent reactivation of the virus.

Treatment can be preemptive and regular monitoring of EBV viral loads is sometimes undertaken to treat primary infection or reactivation with EBV [17].

When an LPT is proven, the curative treatment will be assessed in a multidisciplinary discussion on criteria such as the histological subtype, but also the location and size of the tumor. There are currently no standardized approaches, as therapeutic tools and indications are still poorly established.

A reduction in immunosuppression is often sought as a first-line treatment, but it is most often insufficient and

must be combined with chemotherapy, immunotherapy, immunochemotherapy or cell therapy, or even in more rare cases with surgery and radiotherapy when the tumor remains localized to the original site [18].

Chemotherapy consists of a combination of chemotherapeutic agents such as CHOP alone (cyclophosphamide, doxorubicin, vincristine, prednisone) [19] or, as for the patient here, in combination with rituximab, which is a monoclonal antibody making it possible to strengthen or restore a competent immune system. More recently, therapies specifically targeting proteins located on the surface of cancer cells have been introduced to stop their growth and spread [20].

The initial response to chemotherapy is favorable in PBL with an overall response rate of up to 77% [12]. The prognosis without chemotherapy is poor, with a median survival of 3 months [12].

Conclusion

Despite a constant change in the incidence and clinical picture of PTL, as well as an improvement in their management, these blood disorders still represent a serious complication of transplants.

A better understanding of the risk factors and proliferative mechanisms inherent in PTL will improve the prevention and treatment of these hemopathies.

In this context, the role of the dentist remains essential in the early detection of oral lesions that could be related to extra-nodal PTL.

Authors contribution

I. LEGEARD: rédaction CHEVROLLIER M-A: révision BADER G.: révision.

Conflicts of interests

The authors declare that they have no conflicts of interest in relation to this article.

Informed consent

The authors declare that informed consent not required.

Ethical committee approval

The authors declare that Ethical approval not required.

Source of funding

This research did not receive any specific funding.

References

1. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, *et al.* The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood* 2016;127:2375–2390.
2. Wong GB, Spadafora S, Barbon N, Caputo M. Primary extranodal B-cell non-Hodgkin lymphoma mimicking an endodontic lesion: report of 2 cases. *J Can Dent Assoc* 2013;79:d93.
3. Caillard S, Olagne J, Gautier Vargas G, Cognard N, Muller C, Moulin B. Lymphoproliférations survenant après transplantation d'organes solides. *EMC – Néphrologie* 2017;14:1–11 [Article 18-065-D-20].
4. Batra R, Kaur H, Jindal S. Extranodal large B-cell type aggressive non-Hodgkin's lymphoma. *Indian J Dent* 2014;5:225–8.
5. Caillard S, Lamy FX, Quelen C, Dantal J, Lebranchu Y, Lang P, *et al.* Epidemiology of posttransplant lymphoproliferative disorders in adult kidney and kidney pancreas recipients: report of the French registry and analysis of subgroups of lymphomas. *Am J Transplant* 2012;12:682–693.
6. Ho M, Miller G, Atchison RW, Breinig MK, Dummer JS, Andiman W, *et al.* Epstein-Barr virus infections and DNA hybridization studies in posttransplantation lymphoma and lymphoproliferative lesions: the role of primary infection. *J Infect Dis* 1985;152:876–886.
7. Vega F, Lin P, Medeiros LJ. Extranodal lymphomas of the head and neck. *Ann Diagn Pathol* 2005;9:340–350.
8. Souto GR, Pereira TS, Castro AF, Mesquita RA. Diffuse large B-cell lymphoma, not otherwise specified of the palate: a case report. *J Clin Exp Dent* 2013;5:e287–e290.
9. Castillo JJ, Beltran BE, Miranda RN, Young KH, Chavez JC, Sotomayor EM. EBV-positive diffuse large B-cell lymphoma of the elderly: 2016 update on diagnosis, risk-stratification, and management. *Am J Hematol* 2016;91:529–537.
10. Payet X, Raybaud H, Kipper M, Fino E, Voha C. Lymphome de la lèvre après transplantation rénale : à propos d'un cas. *J Oral Med Oral Surg* 2020;26:2.
11. Carbone A, Gaidano G, Gloghini A, Ferlito A, Rinaldo A, Stein H. AIDS-related plasmablastic lymphomas of the oral cavity and jaws: a diagnostic dilemma. *Ann Otol Rhinol Laryngol* 1999;108:95–99.
12. Hansra D, Montague N, Stefanovic A, Akunyili I, Harzand A, Natkunam Y, *et al.* Oral and extraoral plasmablastic lymphoma: similarities and differences in clinicopathologic characteristics. *Am J Clin Pathol* 2010;134:710–719.
13. Castillo JJ, Bibas M, Miranda RN. The biology and treatment of plasmablastic lymphoma. *Blood* 2015;125:2323–2330.
14. Morscio J, Dierickx D, Nijs J, *et al.* Clinicopathologic comparison of plasmablastic lymphoma in HIV-positive, immunocompetent, and posttransplant patients: single-center series of 25 cases and meta-analysis of 277 reported cases. *Am J Surg Pathol* 2014;38:875–886.
15. Parihar S, Garg RK, Narain P. Primary extra-nodal non-Hodgkin's lymphoma of gingiva: a diagnostic dilemma. *J Oral Maxillofac Pathol* 2013;17:320.
16. Yamada T, Kitagawa Y, Ogasawara T, Yamamoto S, Ishii Y, Urasaki Y. Enlargement of mandibular canal without hyposthesia caused by extranodal non-Hodgkin's lymphoma: a case report. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;89:388–92.
17. Bakker NA, Verschuuren EAM, Erasmus ME, Hepkema BG, Veeger NJGM, Kallenberg CGM, *et al.* Epstein-Barr virus-DNA load monitoring late after lung transplantation: a surrogate marker of the degree of immunosuppression and a safe guide to reduce immunosuppression. *Transplantation* 2007;83:433–438.
18. Patil AV, Deshpande RB, Kandalgaonkar SM, Gabhane MH. Diffuse large B-cell lymphoma (extranodal) of maxillary buccal vestibule. *Journal of oral and maxillofacial pathology: JOMFP*. 2015;19:270.
19. Fohrer C, Caillard S, Koumariou A, Ellero B, Woehl-Jaeglé M-L, Meyer C, *et al.* Long-term survival in post-transplant lymphoproliferative disorders with a dose-adjusted ACVBP regimen. *Br J Haematol*. 2006;134:602–612.
20. Gustafsson A, Levitsky V, Zou JZ, Frisan T, Dalianis T, Ljungman P, *et al.* Epstein-Barr virus (EBV) load in bone marrow transplant recipients at risk to develop posttransplant lymphoproliferative disease: prophylactic infusion of EBV-specific cytotoxic T cells. *Blood* 2000;95:807–814.