Maxillofacial Rosai–Dorfman disease in a newly diagnosed HIV-infected patient

Rosai–Dorfman disease is an uncommon benign proliferation of hematopoietic and fibrous tissue. Its initial manifestations most often include a roughly symmetric, painless, bilateral cervical adenopathy, fever, leukocytosis, and hypergammaglobulinemia, although extranodal disease may develop.\(^1\)–\(^3\) Rosai–Dorfman disease in HIV-infected patients has been previously reported in just three cases.\(^4\)–\(^6\) We report herein the case of a young Venezuelan woman, recently diagnosed with HIV, who had developed Rosai–Dorfman disease with maxillary and malar involvement.

A 56-year-old woman was evaluated at the ear, nose and throat (ENT) service with a three-year history of hard palate swelling with compromise of the right genian region. Physical examination revealed a volume increase in the right side of the face. A considerable hard palate swelling was observed. Laboratory studies on presentation revealed HIV infection (HIV-1 and -2 ELISA tests were positive, and infection was confirmed with the Western-blot test). Multiple lesion biopsies were undertaken. Other laboratory studies were performed; no alterations in complete blood count or chemistry were evidenced. Serology for *Coccidioides immitis*, hepatitis B virus, Epstein–Barr virus (EBV), and cytomegalovirus were positive. The CD4 cell count was 350 cells/\(\mu L\), and the viral load was 10,000 copies of RNA/\(\mu L\). CT-scans showed a significant compromise of the soft tissues in the right maxillary region (including a significant compromise of bone structures). A subtotal therapeutic maxillectomy and biopsy were carried out. The maxillary antirum lateral wall was found to have fibrohistiocytic lesions and inflammatory changes. In the resected tissues, a significant number of large, pale histiocytic cells that contained apparently engulfed lymphocytes or plasmocytes within their cellular borders was observed (emperipolesis; Figure 1). These distinctive large, pale cells — Rosai–Dorfman cells — were S-100 protein-positive by immunostaining and so differ from ordinary histiocytes (Figure 1). CD68 immunohistochemistry was also positive.

Most cases of Rosai–Dorfman disease occur during the first or second decade of life, but any age group can be affected. The youngest patient on first series had congenital sinus histiocytosis with massive lymphadenopathy (SHML), and the oldest developed symptoms at age 74.\(^7\)–\(^8\) However, Rosai–Dorfman disease in HIV-infected patients has been previously reported in just three cases,\(^4\)–\(^6\) the first described in 1991. To our knowledge, this case is the fourth to be reported. Microscopically, there was a pronounced dilatation of the lymph nodes (see Figure 1). The sinuses were occupied by numerous histiocytic cells with a large vesicular nucleus and abundant clear cytoplasm, which may contain lipids and also lymphocytes and plasma cells. The histological key feature of Rosai–Dorfman disease is the presence of various numbers of large, pale histiocytic cells that contain within their cellular borders apparently engulfed lymphocytes or plasmocytes (emperipolesis); these distinctive large, pale cells — Rosai–Dorfman cells — are S-100 protein-positive by immunostaining and so differ from ordinary histiocytes.

Despite its sometimes impressive clinical presentation, Rosai–Dorfman disease is a benign and self-limiting disease, whose treatment is aimed largely at controlling local manifestations (most often by surgical therapy). The microscopic differential diagnosis, particularly in extranodal disease, is at times challenging and can include Langerhans cell histiocytosis, Hodgkin’s disease, non-Hodgkin’s lymphoma, metastatic carcinoma, and metastatic malignant melanoma. Rosai–Dorfman disease with maxillary compromise has been previously reported in four cases (non HIV-infected patients),\(^9\)–\(^12\) and no cases have been reported with malar compromise. In Venezuela, the first case of primary osseous Rosai–Dorfman disease was observed by us in 2002,\(^13\) and to the best of our knowledge this pathology has not been reported again until our current case.
Although numerous case reports concerning Rosai–Dorfman disease have been reported in the literature, few have documented an association with HIV/AIDS. Unfortunately, a consistent etiology for Rosai–Dorfman disease has not yet been found. Immunological relations between Rosai–Dorfman disease and viral infections (human herpesvirus 6 (HHV6) and EBV) have been suggested to explain its etiology;14 HIV could also be one such viral infection.15 Immunopathology of Rosai–Dorfman disease could be linked to viral infections that can create an immunologic environment that will result in the activation of the histiocyte–macrophage system. In this disease the immunohistochemical profile is similar to that of activated macrophages derived from circulating monocytes stimulated by T-lymphocytes following an immunologic challenge.5,14,15 Other studies have indicated that this immunological disturbance is associated with a chronic, but non-specific, infectious state.16 The result of which could reflect an alteration in the process by which histiocytes contact T-lymphocytes for antigen presentation.17,18

The current interpretation of the immunostaining profile of Rosai–Dorfman disease is that SHML cells are functionally activated macrophages, perhaps recently derived from monocytes.15 Related pathologies have already been described in association with HIV, occurring in reactive histiocytosis with hemophagocytosis or in malignant histiocytosis.19,20 In the past, Rosai–Dorfman disease associated with HIV infection has been described as coincidental because it has rarely been reported.4 But, whether or not related, some evidence supports the hypothesis of a relationship between the disease and HIV infection, as has been suggested in cases involving HHV6 or EBV. Immune-mediated diseases, associated with or preceding Rosai–Dorfman, are not rare.4,15 In some studies, about 12% of the patients with this pathology had clinical evidence of one or more immune disorders.12 As was suggested in the first report of an association, we believe that Rosai–Dorfman disease does represent an HIV-associated disease and should be further and more thoroughly studied; it should also be considered in the differential diagnosis of tumors complicating HIV infection.

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References

Chorea in a 29-year-old Nigerian following antimalarial treatment with artesunate

There are about 300–600 million episodes of clinical Plasmodium falciparum infections globally every year. Malaria remains a major cause of morbidity and mortality in tropical countries. Because of the relentless increase in resistance of malaria parasites to conventional drugs, including chloroquine, sulfadoxine–pyrimethamine, and mefloquine, new therapeutic approaches have been developed. The key one among these has been artemisinin-based combination therapy (ACT). Artether, dihydroartemisinin, and arteether. Artesunate is a water-soluble hemisuccinate of dihydroartemisinin. The hemisuccinate group in the molecule confers water solubility and relatively high oral bioavailability. Artesunate is highly active against both the sexual and asexual forms of the four species of Plasmodium that affect humans. The antimalarial action of artemisinins has been attributed to their ability to generate free radicals. The endoperoxide moiety, which is essential for antimalarial activity, is believed to generate free radicals. The endoperoxide moiety, which is essential for antimalarial activity, is believed to generate free radicals. The endoperoxide moiety, which is essential for antimalarial activity, is believed to generate free radicals. The endoperoxide moiety, which is essential for antimalarial activity, is believed to generate free radicals.

Artemisinin is the parent compound that can be variedly modified at the C10 position to produce artesunate, arteether, artether, and dihydroartemisinin, or artelinic acid. Artesunate is a water-soluble hemisuccinate derivative of dihydroartemisinin. The hemisuccinate group in the molecule confers water solubility and relatively high oral bioavailability. Artesunate is highly active against both the sexual and asexual forms of the four species of Plasmodium that affect humans. The antimalarial action of artemisinins has been attributed to their ability to generate free radicals. The endoperoxide moiety, which is essential for antimalarial activity, is believed to generate free radicals within the parasites. These free radicals form covalent bonds with key parasite proteins, such as membrane transporters, thereby impairing their functions. An alternative mechanism of action based on inhibition of the calcium ATPase (sarcoplasmic endoplasmic reticulum cal-
