

Case report

**TUMORAL CALCINOSIS-LIKE LESION IN THE NASAL
SEPTUM IN END-STAGE RENAL DISEASE**

**Mayte Pinilla, Ithzel Maria Villarreal¹, Clara Salas², Pedro Ruiz³, Omar Lafuente⁴,
Cristobal Lopez-Cortijo⁵**

Department of Otorhinolaryngology, Department of Pathology, Department of Radiology
Department of Nephrology.
Puerta de Hierro University Hospital, Madrid Spain

Introduction

A tumoral calcinosis-like lesion or metastatic calcification is a pathologic condition characterized by deposits of calcium-phosphate crystals within otherwise normal soft tissue as a result of hyperphosphatemia with or without concurrent hypercalcemia. There is a hereditary and an acquired possible etiology [1] Metastatic calcification is a well know complication of end-stage renal disease, however the presence of these deposits presented clinically as a nasal lesion is extremely rare [2, 3]

Case Report

A 47-year-old male with end-stage renal disease, a history of chronic renal failure and acute myocardial infarction (with stent implantation), presented himself with a swelling of the anterior nasal septum. Since May 2000 he was treated with hemodialysis. The hemodilutor that is used during these procedures is fragmented heparin. During July 2001, the patient slowly developed a painless swelling in the nasal septum that progressed more rapidly over the last day of that month. On examination, the swelling was a round lesion of approximately 2 cm in diameter and affected the cartilaginous anterior septum in both sides. The remaining nasal septum

Cite: Mayte P, Ithzel M, Clara S, Pedro R, Omar L, Cristobal LC, Tumoral calcinosis like lesión in the nasal septum in end stage renal disease, Journal of Head and Neck physicians and surgeons, 2013;1(1):19-26

did not show any abnormalities. On the surface the lesion had white points and was slightly fluctuant upon palpation. Although the patient did not have fever, a nasal abscess was suspected and the lesion was explored under local anesthesia (lidocaine 2% adrenaline 1:1000.000). A caseous material was evacuated from multilocular tissue. Cultures of this material remained sterile. Radiologic studies with CT scan revealed a focal lesion in the anterior nasal septum with multiple, rounded opacities separated by radiolucent lines in a laminar pattern. (Figure 1a)

The tissue from the biopsy showed a central mass of amorphous and calcified material inside a dense fibrous tissue and bordered by a nodular proliferation of macrophages and multinuclear cells. (Figure 1b)

Laboratory findings presented a severe secondary hyperparathyroidism with hyperphosphatemia but no evidence of increased calcium levels; a Technetium-99 parathyroid scan showed a hyperplasia of both inferior parathyroid glands.

Radiological imaging of large bones revealed no evidence of calcinosis

involving either their soft or periarticular tissues.

The patient had a quick recovery after the operation and intravenous vitamin D was administered to control hyperparathyroidism and later on a parathyroidectomy was performed. During follow-up one year later, the patient presented a minimal lesion without any signs of new deposits in the septal area. At present the patient is alive without nasal symptoms.

Discussion

Tumoral calcinosis is a congenital or acquired defect in calcium metabolism that in the first case is inherited according to a dominant or recessive pattern. It is characterized by tumor-like periarticular deposits of calcium phosphate that are found foremost in the regions of the hip, shoulder and elbow [4]. Some other sites of metastatic calcium-phosphate deposition that have been reported are kidneys, lungs, liver, vessels, stomach, viscera, dura, myocard, pleura, conjunctiva, vocal cords and breasts [2]. In case of being an acquired defect, one of the possibilities that have to be

Cite: Mayte P, Ithzel M, Clara S, Pedro R, Omar L, Cristobal LC, Tumoral calcinosis like lesión in the nasal septum in end stage renal disease, Journal of Head and Neck physicians and surgeons, 2013;1(1):19-26

considered is it being a rare complication of dialysis [4].

Morphologically identical periarticular lesions may be encountered in patients with chronic renal disease and secondary hyperparathyroidism, but most of the patients with these lesions are older than those with tumoral calcinosis [1, 4]. They are described as encapsulate masses, multilobulated of different possible sizes occupied by a creamy dense yellowish material of calcium components. Primary lesions are usually of smaller size than the ones found in patients on dialysis.

Three types of tumoral calcinosis have been described. Type 1 is a tumoral calcinosis not related to disorders of phosphate or calcium metabolism. It is also known as primary normophosphatemic tumoral calcinosis. It usually affects young people, being only a single lesion with low recurrence rate after complete excision. Type 2 is thought to involve a defect in phosphate resorption producing elevated serum phosphate with normal calcium levels. This type known also as a familial hyperphosphatemic tumoral calcinosis may affect teeth, blood vessels, cranium

and diaphysis and recurrence is not rare. Patients with type 3 tumoral calcinosis have an underlying disease such as chronic renal failure with secondary hyperparathyroidism, hypervitaminosis D, milk-alkali syndrome and bone destruction, which lead to soft tissue calcification [4].

There are also tumoral calcinosis-like lesions and vascular calcifications associated with hyperphosphatemia in patients with end-stage renal disease undergoing dialysis [4, 5]. The presence of calcium phosphate deposits in dialysis patients with end-stage renal disease indicates that plasma phosphate levels exceed the precipitation level as a consequence of hyperparathyroidism. Besides hyperphosphatemia with a consequent increase in the calcium-phosphate product (> 70) and secondary hyperparathyroidism, it may also be due to a dynamic osteopathy precipitated by excessive vitamin D and calcium supplementation, exposure to aluminum or parathyroidectomy [6]. Formation of calcium-phosphate deposits can also be facilitated by local factors such as tissue hypoxia, elevation of tissue pH, presence of uremic toxins and local trauma [2]. In

Cite: Mayte P, Ithzel M, Clara S, Pedro R, Omar L, Cristobal LC, Tumoral calcinosis like lesión in the nasal septum in end stage renal disease, Journal of Head and Neck physicians and surgeons, 2013;1(1):19-26

this case the patient can be regarded as suffering from chronic uremia that can also elevate susceptibility for infections.

Repeated micro-trauma can contribute to the formation of the calcium-phosphate deposits in the skin, or in the nasal vestibule (nose-picking) [4, 7]. Up to now this case report is only the third example with nasal septum involvement in end-stage renal disease [2,3,4]. There is however a report of a calcification of the nasal cartilage in an infant who was exposed to warfarin throughout pregnancy and had warfarin embryopathy. It supports the hypothesis that warfarin inhibits Vitamin K-dependent protein that prevent the calcification of cartilage [5]. In our case, fragmented heparin is used in hemodialysis, however heparin does not interfere with vitamin K dependent proteins.

Radiologic imaging may support the clinical diagnosis. Plain radiographs show a calcified homogeneous mass, with a multilobulated appearance. In a CT scan a septated mass with fluid levels may be visible and in MRI scans, signal is low on T1 images and mixed on T2 images with

both high signal related to edema and low signal from calcific deposits.

Histologically, it is described as calcified material surrounded by multinucleated giant cells and mononuclear cells which are CD68 and tartrate-resistant acidic phosphatase (TRAP) and receptor activator of nuclear kappa beta (RANK) positive [8].

Some differential diagnosis includes: osteosarcomas, condrosarcomas, synovial sarcomas, myositis ossificans, dermatomyositis, calcinosis circumscripta, calcific tendinitis and heterotopic ossification [4,6]. Heterotopic calcification may be found accompanying tumoral calcinosis [8].

Risk factors for progressive calcification in patients with chronic kidney disease may include age, duration of dialysis, inflammation, diabetes mellitus, early hyperphosphatemia and an inappropriate calcium load [9].

Treatment must be aimed on reducing the Ca x P product. One option includes the use of low-calcium dialysate to help clearing the calcific deposits, but this measure may exacerbate the secondary

Cite: Mayte P, Ithzel M, Clara S, Pedro R, Omar L, Cristobal LC, Tumoral calcinosis like lesión in the nasal septum in end stage renal disease, Journal of Head and Neck physicians and surgeons, 2013;1(1):19-26

hyperparathyroidism if large amounts of calcium are lost over long periods. A low-phosphate diet, stopping the vitamin D, and calcium supplements may also have some positive results [7,10]. If peritoneal dialysis is the treatment being received it should be changed to hemodialysis, which has less risk of having this complication. One of the most important treatment measures is performing a subtotal parathyroidectomy, which is considered one of the first options when there is a severe hyperparathyroidism. Another surgical possibility, with no doubt, includes a renal transplantation causing reversal of calcinosis with no risk of recurrence. But in our case as well as in other cases of small deposits, the complete excision is the treatment of choice, even though local recurrence is not uncommon [8]. Monitoring the Ca x P and PTH levels is vital in patients undergoing dialysis [6]. It is important to consider that moreover, surgical trauma may stimulate further calcification [4].

We would like to mention other therapeutic concepts for extraosseous calcification that are emerging. Sodium thiosulfate is a clinically established chelator antidote against cyanide

intoxications and it is also used to treat a deleterious disease which causes severe pain and necrotic soft-tissue ulcerations due to calcification of blood vessels and adipose tissue known as calciphylaxis [9,10]. One of the hypothesis of its mode of action is that its molar solubility being more than that of calcium phosphate may potentially interrupt calcium phosphate precipitation in to soft tissue. Nevertheless, its mode of action and optimal administration route are still being studied. Calcimimetics control successfully secondary hyperparathyroidism in patients with end stage renal disease and also lower serum levels of both phosphate and calcium. Still there are studies being held on to prove whether calcimimetics are associated with improvement of meaningful patient outcomes. Strategies to regress or stop the progress of extraosseous calcification are warranted. Loading the system with calcium and phosphate may have very negative outcomes and be of real danger, so the action of novel drugs and other interventions that target clearance mechanisms must be profoundly analyzed and studied [9].

Cite: Mayte P, Ithzel M, Clara S, Pedro R, Omar L, Cristobal LC, Tumoral calcinosis like lesión in the nasal septum in end stage renal disease, Journal of Head and Neck physicians and surgeons, 2013;1(1):19-26

Although our patient has a high risk of developing metastatic calcium deposits, the presence of this calcinosis in the nasal septum was a surprise. An early and adequate diagnosis by radiology and exploration can avoid unnecessary antibiotic treatment and hospitalization. Some complications may include fistula formation and infection, which may produce systemic symptoms.

SUMMARY

Extraosseous tissue calcification in patients with advanced chronic kidney disease undergoing dialysis is a complex, highly prevalent process. Pathological calcification sites may vary, but the localization in the nasal septum is very rare. It is caused by increased calcium phosphate product in the serum, leading to soft tissue calcification. Radiologic imaging help confirm this condition. Adequate control of serum calcium-phosphate levels will diminish the risk of formation or recurrent deposits in these patients.

REFERENCES

1. Sharon W. Weiss, John R. Goldblum. Soft Tissue Tumors. 4th ed. St. Louis
2. Beerens AJ, Stel HV, Middelweerd MJ. Metastatic calciumphosphate deposition in the membranous nasal septum in end-stage renal disease. *Rhinology*, 37,1999,136-138.
3. Alawi F, Freedman PD. Metastatic calcification of the nasal septum presenting as an intraoral mass: a case report with a review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 91, 2001,pp 693-9.
4. Kim S, Kwon Y, Park C et al. Tumoral calcinosis in the nose in a patient with scleroderma: an unusual site for a rare tumor. *J Craniofac Surg*. Jul;24(4), 2013, pp 1483-1484
5. Howe AM, Lipson AH, de Silva M, Ouvrier R, Webster WS. Severe cervical displasia and nasal cartilage calcification following prenatal warfarin exposure. *AM J Med Genet*,71, 1997,391-396.
6. Younes M, Belghali S, Zrour-Hassen S, et al. Complete reversal of tumoral calcinosis after subtotal parathyroidectomy in a hemodialysis patient. *Joint Bone Spine*. Oct; 75(5),2008, pp606-609.
7. Cofan F, García S, Combalia A, et al. Uremic tumoral calcinosis in patients

Cite: Mayte P, Ithzel M, Clara S, Pedro R, Omar L, Cristobal LC, Tumoral calcinosis like lesión in the nasal septum in end stage renal disease, Journal of Head and Neck physicians and surgeons, 2013;1(1):19-26

receiving longterm hemodialysis therapy. J Rheumatol. Feb;26(2),1999, pp 379-385.

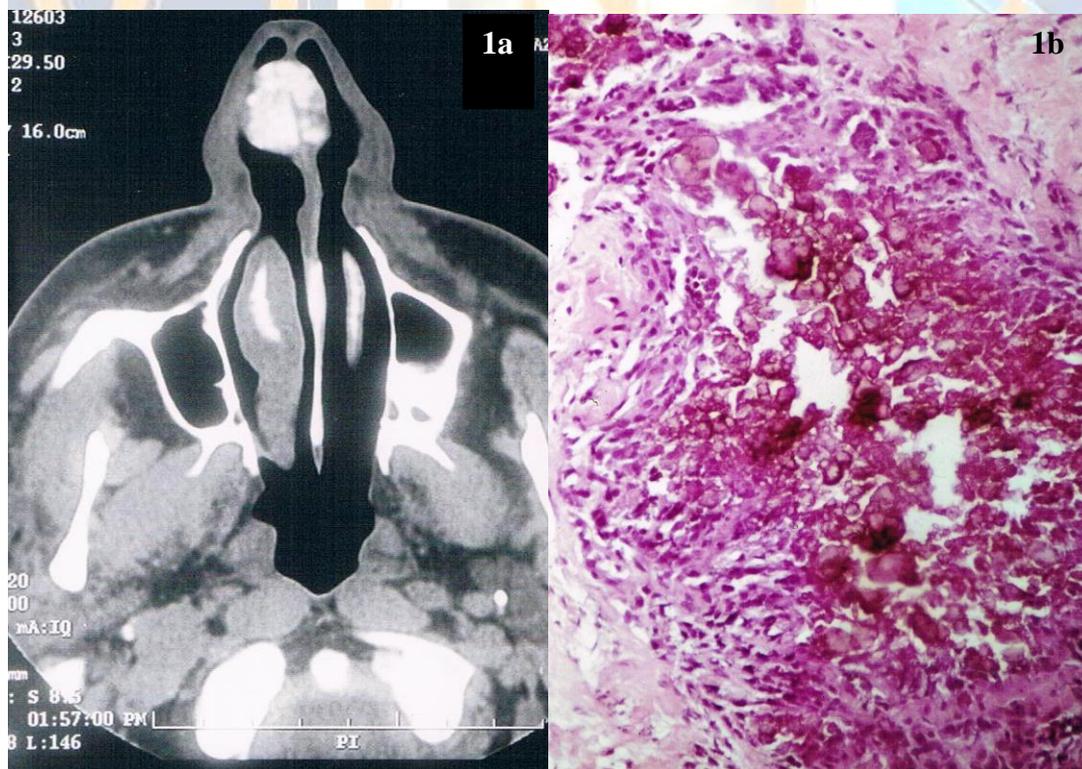
8. Hiramatsu R, Ubara Y, Hayami N, et al. Occurrence of new bone-like tissue formation in uremic tumoral calcinosis. Bone. Feb; 52(2), 2013, pp684-688.

9. Ketteler M, Rothe H, Krüger T et al.

Mechanisms and treatment of extraosseous calcification in chronic kidney disease. Nat Rev Nephrol, Jul 19;7(9), 2011, pp 509-516

10. Yeh SM, Hwang SJ, Chen HC. Treatment of severe metastatic calcification in hemodialysis patients. Hemodial Int, Apr;13(2), 2009, pp 163-167

FIGURES



Cite: Mayte P, Ithzel M, Clara S, Pedro R, Omar L, Cristobal LC, Tumoral calcinosis like lesión in the nasal septum in end stage renal disease, Journal of Head and Neck physicians and surgeons, 2013;1(1):19-26

Figure 1a. Soft tissue mass with extensive areas of calcification that affects the anterior septal cartilage (Axial CT scan)

Figure 1b. Histopathologic examination with a tumoral calcinosis in active phase (hematoxylin and eosin stain x200)

Conflict of interest – Nil

Acknowledgements- Nil

Support- Nil

Correspondance:

Mayte Pinilla

C/San Restituto

72C, 6-4 28039

Madrid, Spain

Phone: + 34 629810134



www.jhnps.weebly.com

Cite: Mayte P, Ithzel M, Clara S, Pedro R, Omar L, Cristobal LC, Tumoral calcinosis like lesión in the nasal septum in end stage renal disease, Journal of Head and Neck physicians and surgeons, 2013;1(1):19-26