BIRT-HOGG-DUBÉ SYNDROME

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Abstract

The purpose of this case report is to discuss the presentation, diagnosis, and additional medical symptoms of Birt-Hogg-Dubé syndrome in an adult outpatient. The characteristic manifestations of this disease are necessary for clinicians to recognize as they can seem unrelated and be treated separately without further investigations for a genetic cause. The literature states that it primarily involves three organ systems but given the limited information on this disease, it is possible that the mutation is more widespread than originally thought. In addition to the usual symptoms of BHDS, this patient had other conditions of interest involving the thyroid, parathyroid glands, and facial bone tumors.

Introduction

Birt–Hogg–Dubé syndrome (BHDS) is a rare multi-system genetic condition primarily affecting the lungs, kidneys, and skin. UpToDate reports that only 200 families worldwide have been identified to have the mutation resulting in BHDS.[1] Presentations occur in adulthood and include lung cysts, spontaneous pneumothoraces, kidney tumors (benign and cancerous), and skin lesions. The mutation can be traced back to the FLCN gene and is inherited in an autosomal dominant pattern. This case of a patient with BHDS is worth interest because they also had a history of hypothyroidism, hyperparathyroidism, parathyroidectomy for parathyroid adenomas, and bilateral maxillary brown's tumors. These conditions have been recorded in relation to BHDS but due to lack of sample size, there is not enough literature to confirm that the FLCN mutation effects more than the original triad of organ systems. It is critical to arrive at the correct diagnosis of BHDS so that patients can counsel other family members to seek the appropriate screening tests and treatment.

Case

A 56 year old female with a history of Hashimoto's thyroiditis was seen in clinic because she had shortness of breath, wheezing, chest pain, and last night woke from her sleep gasping for air. A chest X-ray

was ordered in clinic and showed a large spontaneous pneumothorax in the right lung prompting her transfer to the ED. Blood pressure in right arm was 169/110 and 144/87 in the left arm. A chest tube was inserted and follow up X-ray showed that it had resolved and that there was atelectasis changes in the right lung base and a small amount of subcutaneous emphysema. She was discharged the next day and no further investigations were ordered. Months later, she told her doctor that a cousin was recently diagnosed with BHDS and a chest CT was ordered. Results showed a small thin-walled 2 cm cyst and an additional 8 mm cyst both in the right lower lobe. She also had a history of dermatofibroma excisions and some small skin lumps on her neck. The pulmonary findings, prior history of benign skin lesions, and family history of BHDS raised suspicions that she also had BHDS and was referred to the Hereditary Cancer Clinic. Genetic testing confirmed that she did carry the familial FLCN c.59deIT mutation and was formally diagnosed with BHDS.

The patient had high levels of calcium on bloodwork and an ultrasound of her thyroid was ordered. It showed a left thyroidal nodule that was 9 x 5 x 5 mm and posterior to the lower pole of the right lobe of the thyroid gland was a lobulated nodule measure 6.7 X 2 x 3.4 cm. They were bilateral parathyroid adenomas that were causing hyperparathyroidism. On further imaging, the oral maxillofacial surgeon also noted that she had bilateral maxillary tumours. The endocrinologist identified the hyperparathyroidism as the cause of Brown's tumors in her maxillae. Medical intervention was given and the Brown's tumors regressed. However, the tumour of the right maxilla had infiltrated the hard palate and required surgical excision for which she will be receiving. The patient had also received a parathyroidectomy for long term management.

The optimal screening modality for the patient was to receive yearly MRI scans of her kidneys to assess for renal tumours, and to have full body skin examinations to evaluate for melanoma. She was also advised to avoid cigarette smoking and high ambient pressures which could precipitate a spontaneous pneumothorax. The skin lesions of BHDS are benign and are treated only for cosmetic reasons. Once they have developed, they are permanent and no curative treatment is currently available. Surgical and CO2 laser treatments can be used to remove the skin lesions but this is only a temporary fix and the lesions often return over time.

Discussion

It is critical for clinicians to ask screening questions and order appropriate investigative tests for patients who present with a non-traumatic pneumothorax. A family history of pneumothoraces or prior medical history of pneumothoraces, kidney tumours and skin lesions, would all be indications to order a chest CT once the patient is stable. Understanding the cause of the spontaneous pneumothorax (SP) is critical for BHDS patients as they should be cautioned about the potential dangers of air travel. Furuya et. al state that pulmonary cysts are seen in 80-100% of BHDS patients and are associated with SP which have a recurrence rate of 75%[2]. Most patients are asymptomatic and symptoms only appear when a SP is present.[3] The atmospheric pressure changes that occur during air travel will expand and compress pulmonary cysts. Under enough stress, this can cause the cysts to rupture and cause a pneumothorax.

PubMed provides three results[4, 5, 6] when searching "Birt-Hogg-Dubé Syndrome AND parathyroid." PubMed also provides two articles that report a BHDS patient with Hashimoto's thyroiditis[7,8]. It is possible that there is thyroid and parathyroid involvement with the FLCN mutation and should be investigated further. The parathyroid adenomas increased parathyroid hormone causing hyperactivity of osteoclasts and resulted in Brown's tumours. Brown's tumors are common benign lesions however, the involvement of facial bones has only been reported in 4.5% of cases.[3] Tumors of the maxillofacial region are more likely to affect women than men, with a reported female: male ratio of approximately 1.7:1 and mean age at diagnosis of 34 years.[4]

Conclusion

Given the rarity of BHDS and limited research, there is still uncertainty that the FLCN mutation is restricted to the skin, lungs, and kidneys. Further studies are necessary to understand if it plays a role in thyroid and parathyroid pathologies. It is worthwhile for clinicians within the region to educate themselves on the symptoms of BHDS given that a family has been identified and there is a 50% chance of the condition being inherited by children. For patients with no known family history, it is especially important for them to receive this diagnosis so that they can counsel other family members to monitor their health and request the appropriate screening tests.

Works Cited

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