

DYKE-DAVIDOFF-MASSON SYNDROME: AN ENDOCRINE PERSPECTIVE

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ABSTRACT

Dyke-Davidoff-Masson syndrome (DDMS) represents a severe disease that is caused by brain anomalies of different mechanisms early in life during fetal period or within first years after birth. This is a brief point of view of DDMS through an endocrine perspective. In DDMS, low TSH (thyroid stimulating hormone) hypothyroidism is part of a variable cocktail of endocrine anomalies like pituitary insufficiency that actually seem less relevant opposite to massive neurological damage which marks the clinical picture. Overall, the most spectacular anomaly and the most specific in DDMS is the imaging aspect of the brain hemiatrophy. The syndrome itself, even with a very low prevalence in general population (the level of statistical evidence is case report or series), has a heterogeneous presentation and a large area of clinical combo involving not only neurological field. On the other hand, cerebral hemiatrophy (also a rare neuroimaging finding) may have other causes, either acquired or congenital. Seizures induced by brain damage may be presented long before the imaging recognition of the syndrome is actually done. The endocrine disturbances vary and they may be subtle like central hypothyroidism or life threatening like adrenal crisis due to secondary adrenal insufficiency.

Overall, DDMS represents a complex challenge from severe neurological deterioration to neuro-imagery features centered on the brain hemiatrophy to skin and bone anomalies as well as endocrine disorders which are either deficiency of pituitary hormones or diabetes mellitus and autoimmune thyroiditis. Early recognition is useful for long term prognosis, a multidisciplinary approach is essential. Underlying causes and specific clusters of classification are still running under a large shadow of unknown data.

Keywords: Dyke-Davidoff-Masson syndrome, hypothyroidism, cerebral hemiatrophy

INTRODUCTION

Dyke-Davidoff-Masson syndrome (DDMS) is a severe disease that is caused by brain damage of different mechanisms early in life during fetal period or within first years after birth (1). Cerebral anomalies may be caused in some cases by cerebral vessels congenital damage in addition to skin vascular malformations, bones anomalies at the level of skull and sinuses, face, peripheral skeleton (called Legg-Calve-Perthes-like disease) and even autoimmune conditions like insulin dependent diabetes mellitus and thyroiditis.

OBJECTIVE

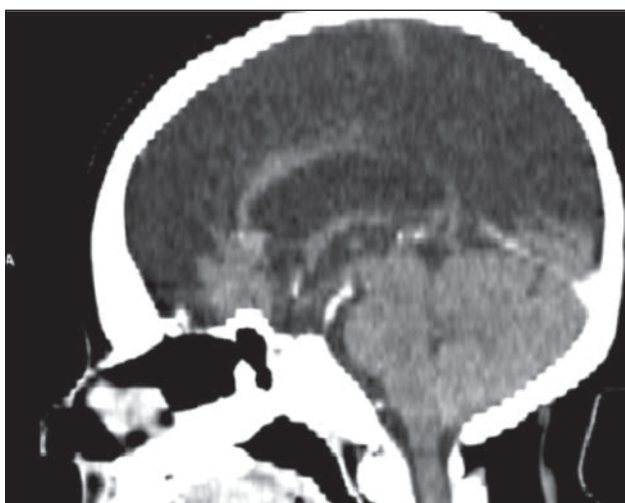
This is a brief point of view starting with a medical image of a prior unpublished DDMS case (respecting the anonymity of the medical data).

MEDICAL IMAGE

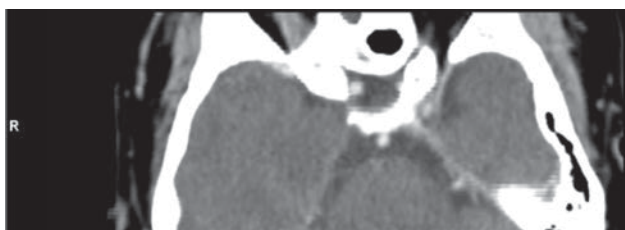
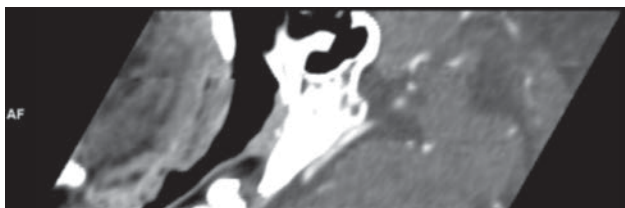
This is the computed tomography (CT) aspect of the brain (Figures 1, 2) and pituitary gland (Figures 3, 4) of a 19-year old non-smoker male diagnosed with DDMS syndrome soon after birth presenting with left cerebral atrophy which

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suffered a liquid transformation as well as empty sella appearance at imaging scan. In addition to multiple neurological issues, the patient associates GH (growth hormone), prolactin and TSH (thyroid stimulating hormone) deficiency which were recognized during childhood.



FIGURES 1 and 2. Computed tomography (CT) aspect of the brain



FIGURES 3 and 4. Computed tomography (CT) aspect of the pituitary gland

DISCUSSION

DDMS- associated hypothyroidism is an atypical one, among various causes like iodine – deficiency related goitre and chronic thyroiditis (2,3). Actually, Hashimoto disease of the thyroid represents the most common cause of thyroid hormones insufficiency in paediatric population, as a single entity or (less frequent) in addition to autoimmune damage of the adrenals etc. (4,5). Central hypothyroidism is found rarer than primary forms and it may be related to genetic causes or to pituitary tumours/masses/neoplasia of secretor or non-secretor pattern, usually of more than 1 centimetre diameter which are rarely detected as incidentaloma and rather as hypothalamic-hypophysis hormones deficiency, including diabetes insipidus, or optic chiasm anomalies etc. (6-8).

In DDMS, low TSH hypothyroidism is part of a variable cocktail of endocrine anomalies that actually seem less relevant opposite to massive neurological damage which marks the clinical picture (1,9). Cerebral anomalies may be caused in some cases by cerebral vessels congenital damage in addition to skin vascular malformations, bones anomalies at the level of skull and sinuses, face, peripheral skeleton (called Legg-Calve-Perthes-like disease) and even autoimmune conditions like insulin dependent diabetes mellitus and thyroiditis (10). Low TSH levels differentiate an autoimmune thyroiditis – associated hypothyroidism to an empty sella-related one (11). Secondary adrenal insufficiency, but not autoimmune Addison disease, was also reported in a limited number of cases which may become life threatening if it is unrecognized (12,13). However, the most frequent endocrine autoimmune DDMS associated conditions remain diabetes and thyroiditis (14).

In this syndrome, endocrine disorders may exceptionally include dwarfism due to GH deficiency which may be, otherwise, caused by other genetic conditions, neonatal trauma, large pituitary masses etc. (15-17). Prolactin anomalies in DDMS may go in both ways: up due to lifelong requirement of neurological medication like against epilepsy crises or down as part of a severe pituitary insufficiency (1,18). Also, a certain correlation with schizoaffective disorders in DDMS have been reported and the specific medication for them may induce a high prolactin level (19). Drug induced hyperprolactinemia in children and youth needs to be differentiated from a prolactinoma, renal failure, severe myxedema, thoracic trauma etc. (20-22).

In addition to neurological, vascular and endocrine disturbances, oral anomalies have been re-

ported like delayed tooth eruption, teeth hypoplasia and even taurodontism etc. (23). Other endocrine causes of oral anomalies (not necessarily related to neurological syndromes) are presented in gigantism/acromegaly or severe vitamin D deficiency in early childhood years etc. (24,25).

Some cases of DMMS are actually recognized during teenager period of time even symptoms like convulsions are persistent since early years after birth (26,27). The use of neurological medication, long standing uncontrolled hyperprolactinemia, food intake anomalies, low IGF-1 (insulin-like growth factor) impair optimal peak bone mass achievement and eventually bone turnover and bone mass (28-30).

Brain anomalies may be masked by headache especially in cases with late establishment of the DMMS diagnosis during adult life (31,32). Headache in endocrine conditions may be caused in both pediatric and adult population by large pituitary tumors or high blood pressure due to endocrine hyper-production of hypophysis and adrenal tumors like GH or cortisol (33,34).

Overall, the most spectacular anomaly and the most specific in DMMS is the imaging aspect of the brain with hemiatrophy (35). The DMM syndrome itself, even with a very low prevalence in general population (the level of statistical evidence is case report or series), has a heterogeneous presentation and a large area of clinical combo involving not only neurological field (36). On the other

hand, cerebral hemiatrophy (also a rare neuroimaging finding) may have other causes, either acquired or congenital (37,38). Seizures induced by brain damage may be presented long before the imaging recognition of the syndrome is actually done (39,40).

CONCLUSIONS

DMMS represents a complex challenge from severe neurological damage to neuro-imagery features centered on the brain hemiatrophy to skin and bone anomalies and endocrine disorders in some cases like deficiency of pituitary hormones. Early recognition is useful for long term prognosis, a multidisciplinary approach is essential. Underlying causes and specific clusters of classification are still running under a large shadow of unknown data.

Disclaimer

The medical images were not previously published. However, the case data were partially introduced at ENDOPED International Congress 2020 as poster presentation and then selected as oral presentation. The abstract was published as the following citation: Dumitrascu A, Dumitrescu C, Valea A, Carsote M. Central Hypothyroidism: The Endocrine “Memory” for Dyke-Davidoff-Masson Syndrome. *CEACR (Central European Annals of Clinical Research)*. 2020;2(2):16.

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