Brain MRI is an essential diagnostic tool when approaching the management of a patient with hypopituitarism. Although some H-P abnormalities on Magnetic Resonance Imaging (MRI) have been strongly associated with hypopituitarism, a correlation between specific H-P findings and the severity and timing at onset of different pituitary deficits is less clear. Additionally, due to the rarity of the condition, the distinctive H-P neuroimaging features of children with Septo-Optic Dysplasia (SOD) have only been reported in small case series.

AIM

The aim of this study was to evaluate the range of H-P structural abnormalities and the endocrine morbidity of children with SOD compared to those with isolated Multiple Pituitary Hormone Deficiencies (MPHD) (without optic nerve and midline brain abnormalities) and to those with isolated Optic Nerve Hypoplasia (ONH).

METHODS

- The number of pituitary deficits was scored by the Endocrine Morbidity Score (EMS) ranging from 1 (one pituitary deficit) to 5 (panhypopituitarism).
- Magnetic resonance images were reviewed by one experienced neuroradiologist.
- The following H-P abnormalities were reported:
  a. absent/hypoplastic/enlarged Anterior Pituitary (AP)
  b. absent/hypoplastic/enlarged/ectopic Posterior Pituitary (PP)
  c. absent/hypoplastic/interrupted/thickened Pituitary Stalk (PS).
  d. PS Interruption Syndrome (PSIS) [Small AP, Ectopic PP (EP) and PS Absence (PSA)].

RESULTS

**Summary of Main Findings**

- Of SOD patients, 39/171 (23%) did not develop hypopituitarism over a median (25th,75th centiles) follow-up of 6.20 (3.41, 8.06) years, although 73% of them had a SAP (Table 2).
- Half of the patients with ONH had SAP (Table 2), but preserved pituitary function at 10.22 (5.96, 12.98) years of follow-up.
- Compared to SOD, MPHD patients developed the first deficit earlier (Figure 1A).
- MPHD patients were significantly more likely to manifest each individual anterior pituitary deficiencies and to develop these earlier (Figure 1B), with a higher prevalence of EPP and PSIS (Table 2).
- Diabetes Insipidus (DI) (Figure 1B) and PP Absence (PPA) (Table 2) were more frequent in SOD.
- The time to first deficiency was significantly associated with the number of pituitary deficits that subsequently developed (HR 1.59 [1.36, 1.85]) (Figure 2) and with the presence of EPP [Hazard ratio 2.11 (1.41, 3.15)] and PPA [Hazard ratio 2.54 (1.53, 4.21)], in both groups.
- In SOD only, there was an association between PSA and ACTH, GH and TSH deficiencies, as shown by the interaction Hazard ratio of 3.02 (1.16, 7.84), 2.7 (1.10, 6.61) and 3.04 (1.23, 7.56), respectively.
- Among DI patients, 6/26 (23%) SOD and 3/5 (60%) MPHD had a normal PP and 3/26 (11.5%) SOD and 1/5 (20.0%) MPHD had EPP. Among patients without DI, 18/128 (14.1%) SOD and 2/45 (4.4%) MPHD had PPA.
- Unusual MRI abnormalities (pituitary enlargement or pituitary stalk thickening) were documented in SOD only (Table 2).

**CONCLUSIONS**

- SOD patients present with a wide spectrum of radiological H-P abnormalities and with heterogeneous endocrine phenotypes; whilst MPHD tend to develop multiple anterior pituitary deficits at early stages of life with a higher prevalence of EPP and PSIS.
- PSA is associated with the development of specific anterior pituitary deficiencies in SOD only.
- SAP and PPA have low predictive value for the development of anterior and posterior pituitary deficits. MRI findings can predict the development of endemic deficits; only to some extent, hence life-long surveillance is essential in all groups.